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FURTHER CLINICAL INVESTIGATIONS INTO THE DISEASES ARISING IN CONSEQUENCE OF A DEFICIENCY IN THE FAT-SOLUBLE A FACTOR *

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COPENHAGEN, DENMARK

My description of the diseases occurring in children from a deficiency in the fat-soluble A factor was quickly acknowledged by those physiologists who were working at vitamin problems. This was due to the close parallel, which in many respects exists between the disease I have observed in children and the condition that can be produced in young rats, by keeping them for a long time on a diet poor in the fat-soluble A factor but otherwise adequate. With clinicians it was a different matter. Although nearly a decade has passed since I published my first contributions on this subject, there are still many clinicians, especially in Germany, who have never appreciated the fact that the absence of the fat-soluble A factor gives rise to a well defined disease just as, for example, the absence of the C factor does. There are, however, many German authors who trace a connection between the deficient growth of the children and the great prevalence and serious course of tuberculosis and similar diseases during the war on the one hand, and the lack of the proper food substances (i. e., those containing the fat-soluble A factor) on the other, but that it is an indication of the absence of the fat-soluble A factor is usually not understood or not alluded to. With regard to the characteristic symptom, xerophthalmia, it is stated by many that this condition is not caused by a deficiency in the fat-soluble A factor alone but is merely the result of general marasmus.

Besides the support accorded by English and American physiologists, my account and interpretation of the condition received very substantial confirmation from the investigation into xerophthalmia in Denmark which, after the appearance of my contributions, was undertaken by Olaf Blegvad at the instance of the Danish Ophthalmological Society.

* Received for publication, Oct. 4, 1924.

* From the Children's Department of Rigshospitalet, University of Copenhagen.

* Read before the Third Northern Pediatric Congress, Christiania, Norway, July, 1924.

A total of from 600 to 700 cases was collected, of which 434 had keratomalacia, my previously reported cases being included in these, and this large amount of material exhibited in nearly every particular the same features as those cases which I had originally described.

It is no new idea that xerophthalmia is merely due to general marasmus; even the earliest ophthalmologists who first observed keratomalacia regarded it as an indication of a severe morbid derangement of nutrition, a symptom of the moribund state. In an article emanating from the Reichanstalt für Mutter—und Säuglingsfürsorge in Vienna by Eugen Stransky,[1] this view is further supported on the basis of six of his own cases and some previously reported by other authors. The information concerning the latter is so incomplete that it is impossible to deal with them, and I must therefore confine myself to the author's six cases.

Stransky himself considers that one of them was caused by the absence of the fat-soluble A factor, for the patient recovered rapidly on receiving cod liver oil and butter. In the other five patients, all of whom died, there could not, in the author's opinion, be a lack of the fat-soluble A factor, partly because the children had received a quantity of it in their food and partly because the eye lesion became worse in spite of the liberal allowance of cod liver oil and butter.

When we consider the explanation I have advanced as to how the deficiency in the fat-soluble A factor arises, we must assume that Stransky's other cases of xerophthalmia are likewise due to absence of the fat-soluble A factor. I will briefly recapitulate what I have said about deficiency in the fat-soluble A factor and xerophthalmia.[2]

My investigation was comprised of seventy cases of xerophthalmia (not twenty-three as Stransky states). I have examined and treated all the patients myself, and took most careful histories. I even followed some of them for a long period of time before the xerophthalmia occurred. In the majority of cases the diet had been poor in the fat-soluble A factor for a considerable time, and it was the principal cause of the appearance of the xerophthalmia in these cases. But a diet entirely devoid of the fat-soluble A factor, as in the animal experiments, was found only in a small number of cases, for even centrifuged milk and buttermilk usually contain some of the fat-soluble vitamin. In some instances the children had received fresh milk, and even if this had only been in small quantities and the milk had often been stale, pasteurised and then diluted half or more with water and boiled with

1. Stransky, Eugen: Klinische Beiträge zur Frage der Aetiologie der Keratomalacie, Jahrb. f. Kinderh. **104**:183 (Feb.) 1924.

2. Bloch, C. E.: Clinical Investigation of Xerophthalmia and Dystrophy in Infants and Young Children, J. Hygiene **19**:283 (Jan.) 1921; ibid, Blindness and Other Diseases in Children Arising from Deficient Nutrition, Am. J. Dis. Child. **27**:139 (Feb.) 1924.

flour to make gruel, operations which expose the milk to oxidation and consequent destruction of the fat-soluble A factor, it would be likely that a portion of this factor was preserved and that the child had received it. It was, therefore, impossible to explain the occurrence of the xerophthalmia in all cases on the score of deficiency in the fat-soluble A factor in the diet alone.

On going over all these cases carefully I found that, besides the deficient supply and assimilation of the fat-soluble A factor, the appearance of xerophthalmia depended on two other conditions: namely, growth and infectious diseases, I therefore advanced the theory:

That the fat-soluble A factor is made use of in growth, which statement is in agreement with all the animal experiments.

That the fat-soluble A factor is also used in infections, particularly the chronic ones of long duration, which theory has subsequently been accepted by most investigators and also by a number of clinicians. Moreover, later investigations into the amount of antibodies in the blood in xerophthalmia show that my theory is right.

The organism's lack of the fat-soluble A factor, of which xerophthalmia is the characteristic symptom, may therefore arise partly from a deficient supply, that is, food poor in the fat-soluble A factor, or diseases of the digestive tract which hinder digestion and the absorption of this factor, and partly from increased consumption during the periods of growth and in wasting infections.

Since 1918, when I last reported my cases of xerophthalmia, I have had twenty additional cases. The course of all of them has been the same as that of my earlier patients.

Passing on to Stransky's last four cases, we find that the patients were small children. One of them was debilitated from birth (weight at birth 1,600 gm.), all had chronic digestive trouble, three of them had diarrhea, in one case dysenteric, one also had extensive pneumonia, another also had a chronic septic condition with subcutaneous hemorrhages, a third had a pustular skin eruption accompanied by abscesses and cellulitis, hemorrhages in the skin and pneumonia, and all of them exhibited rapidly progressive marasmus when the eye lesion occurred; they died nine, four, seven and three days, respectively, after the eye disease was diagnosed.

There was no proof that the children had received a diet rich in the fat-soluble A factor before the disease developed; the information obtained points rather in the opposite direction.

From the explanation I have put forward of the occurrence of the deficiency in the fat-soluble A factor, it will be seen that such may have applied to Stransky's cases. These children consumed a lot of the fat-soluble A factor; but even if it was supplied to them they could not absorb it, and we could hardly expect any effect on the xerophthalmia from the administration of cod liver oil and butter.

In only one of the patients is the condition unusual, and it does not agree with previous experience, xerophthalmia having occurred in association with uncomplicated inanition from congenital stenosis of the duodenum. The child died nearly three months after birth. The patient was admitted to the hospital five days before death occurred, at which time the child was greatly emaciated; a leukoma adherens was observed on the left eye, and a central corneal ulceration on the right eye. The characteristic symptom, xerophthalmia, was not mentioned. This was probably a case of keratitis of some other nature and cause.

I consider, therefore, that I can assert, that xerophthalmia has not yet been demonstrated in any other disease, and that it is the characteristic symptom of the organism's lack of the fat-soluble A factor.

While xerophthalmia is a characteristic symptom, the other symptoms which I have found to follow deficiency in the fat-soluble A factor are not particularly specific. Inhibition of growth, loss of weight, depressed mental and bodily vitality and impaired immunity may be found more or less pronounced in all diseases accompanied by a chronic debilitated state.

On a previous occasion I [3] remarked that we might expect xerophthalmia to occur in those liver diseases that were associated with impaired digestion and absorption of fats. In the older literature, a few such cases are met with in adults, and Blegvad has recently observed xerosis in a patient with cancer of the pancreas which occluded the bile duct. Hitherto such cases have not been described in children.[4] The two following cases may therefore be of interest and, moreover, in several respects, they throw light on the disease due to the fat-soluble A factor deficiency and its relation to rickets.

REPORT OF CASES

CASE 1.—G. H., a girl, aged 9 months, was born July 5, 1923. The patient was admitted to hospital, March 25, 1924, and died, March 27.

The child was born six weeks before full term (weight at birth 1,500 gm.). She had always been artificially fed, with increasing quantities of diluted fresh milk. For the first few months there was a slow increase in weight up to 3,250 gm., and then no change for several months. Three weeks previous to admission the child had lost weight and then weighed 2,500 gm.

The infant was jaundiced from birth. The stools were usually light but were stated to have been normal in appearance otherwise.

The child then became much worse and a few days before admission xerosis was observed in both eyes.

On admission, the child was moribund, emaciated, deeply jaundiced, with dry cornea and xerosis spots on the conjunctivae. The temperature was 38.2 C. (100.8 F.). Albumin and pus were present in the urine.

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3. Bloch, C. E.: Proc. M. Soc., Copenhagen, Dec. 1916.

4. After this was written, similar cases were reported from Pirquet's Universitäts Kinderklinik, Vienna. Wagner, Richard: Xerophthalmiebereitschaft und Leberfunktion, Wien. med. Wchnschr. **74**: 1924.

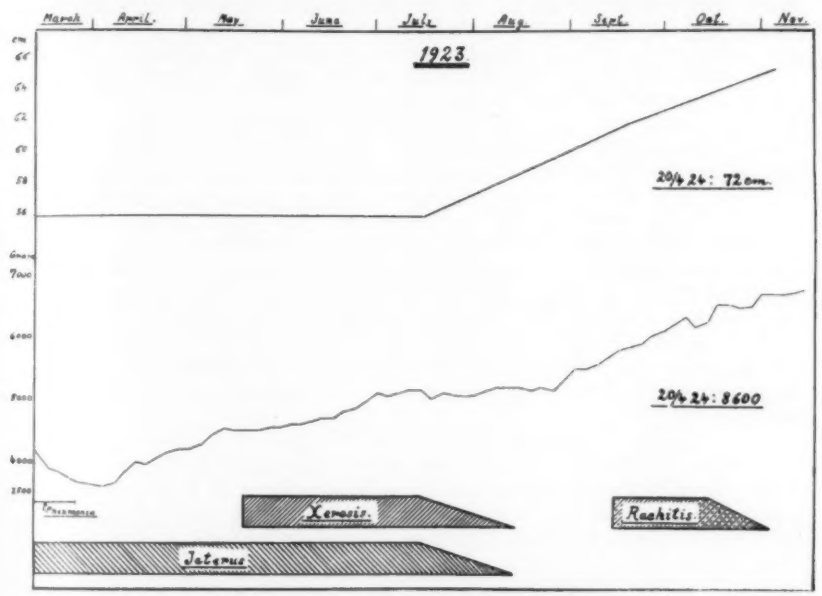
The child died thirty-six hours after admission. At necropsy, cirrhosis of the liver, cystoureteritis, pyelonephritis and atrophy of the organs was found. There were no signs of osteoporosis or of rickets.

Comment.—The child had received the fat-soluble A factor in her diet the whole time, and at first drank fairly well, but on account of the liver disease too little of the fat-soluble A factor was assimilated.

The course of the disease was the usual one for fat-soluble A factor deficiency, first, a slow increase in weight, then a state of equilibrium for a long period followed by loss of weight. The infection started at the same time, in this case of the urinary tract, and shortly after xerophthalmia appeared.

CASE 2.—R. N., a boy, was born Jan. 1, 1923. The child was admitted to hospital, March 14, of the same year, and discharged Feb. 13, 1924.

The patient was premature. The weight at birth was 3,250 gm. The mother nursed him for five months, until June 1. For the first two months he had



Upper curve shows length, lower curve weight in Case 2.

breast milk only, but later different dilutions of fresh cow's milk. The patient had jaundice at birth which increased later. He was admitted to the hospital because of pneumonia and jaundice.

The patient was fairly well nourished, but small, feeble and backward in development. The weight was 4,250 gm., the height, 56 cm. He had fever for ten days and was run down from the effects of the pneumonia which resulted in a considerable loss in weight; on August 4, he weighed 3,700 gm. At this time there was a tendency to hemorrhage of the skin and mucous membranes.

The child gradually recovered but the jaundice remained unchanged. A marked yellow staining of the skin and sclerotics continued, the urine was bile stained and the feces free from bile pigment. The liver and spleen were not enlarged. The Wassermann and Pirquet tests were negative. The examination of the blood gave practically a normal result.

After the pneumonia had disappeared, the mother nursed the child two or three times daily, whereby it obtained from 200 to 400 c.c. of milk per day,

and he received in addition from 500 to 600 c.c. of malt soup or buttermilk gruel. The child increased in weight to 4,600 gm., on May 14, but continued to be feeble and the height was unaltered. Only the cranium was increased, the circumference measuring 1.3 cm. more.

May 24, xerosis was detected in both conjunctivae. The corneas were intact.

June 1, the mother had to cease nursing the child, although she was healthy and strong. During the whole period of nursing she drank about 1 liter of fresh milk daily.

From May 24, the child received two-thirds part fresh milk, malt soup and gruel made with undiluted fresh milk. In addition, he was given cod liver oil 2.5 gm., which was continued during the next seven or eight months.

The xerosis and jaundice remained the same for the whole of June.

The weight kept constant until July 19, after which it increased to 5,150 gm. on August 12, while the diet contained malt soup. The circumference of the cranium enlarged further by 1.7 cm. but the height remained unchanged.

In the beginning of July, the feces were more colored and the jaundice slowly diminished. Afterward the xerosis also declined little by little; on July 17, small dry spots remained close to the borders of both eyes on the nasal and temporal aspects.

During August, the jaundice completely disappeared and on August 21, no definite xerosis could be seen.

The weight and height were practically unchanged during July and August.

In September there was a sharp increase in weight and growth. On September 20, the child's weight was 5,900 gm.; the height, 62 cm. Hitherto rickets had not developed. Softening of the cranial bones, a rosary and other epiphyseal enlargements now developed.

Roentgen-ray examination showed, August 31, that the diaphyses of the radius and ulna were slightly fringed; September 18, a similar condition continued; on September 21, there were marked rachitic changes; the ends of the diaphyses were excavated, cup shaped, fringed, and there were layers of periosteal deposits. There was no atrophy of the bones; on November 3, the rickets was healed.

During October and November the rickets disappeared and there was steady improvement. November 11, the weight was 6,800 gm.; the height, 65.5 cm.

April 10, 1924, the patient passed through a new attack of pneumonia. It was somewhat backward in developing but there were no demonstrable abnormalities. The weight then was 8,500 gm.; the height, 72.5 cm.

COMMENT

In Case 2 likewise, jaundice existed from birth, which was severe and associated with light colored feces in the first 6 or 7 months of the child's life, after which it gradually declined but did not entirely disappear until the child was 8 or 9 months old.

The child was vigorous from birth, was breast fed by his mother, grew and throve fairly well for the first two months. He then developed pneumonia, but in spite of abundant nourishment, breast feeding and other milk, the patient did not grow. There was some increase in weight only in those periods in which the child received some carbohydrates, and he became more and more feeble and dull.

During the last days of May, a time of the year when xerophthalmia seldom occurs, the child developed xerosis in both eyes. Cod liver oil was now given in addition to the milk diet containing the fat-soluble A

factor. The xerosis and arrested growth, however, remained the same for two or three months. Not before the feces became bile stained and the jaundice disappeared did the xerosis gradually pass away and the child begin to grow.

When the child was aged 9 months, the xerosis and jaundice had entirely gone and he had grown and begun to develop. At the same time severe rickets appeared at a period of the year (September) when florid rickets is rare, despite the fact that the child had lived under the best conditions and in the sunlight and had received cod liver oil the whole time. The rickets disappeared during the two following autumn months; no change had been made in the child's food or environment.

An examination of the child the following spring showed that he had made further development, and that there was neither jaundice, xerosis nor rickets present.

SUMMARY

These two patients thus show that the fat-soluble A factor is digested and assimilated, together with the fats. If fat is not digested the fat-soluble A factor is not absorbed from the intestine.

A fact which I have previously pointed out is also elucidated. While the organism is suffering from deficiency in the fat-soluble A factor, i. e., while there is arrested growth and xerophthalmia, rickets does not occur. Not until the fat-soluble A factor deficiency is remedied and growth takes place does rickets appear.

In my earlier patients, florid rickets did not as a rule occur after the xerophthalmia had disappeared, but the present case differed from my previous ones in the sudden and marked growth. One gets the impression that the calcification of the rapidly growing osseous tissue could not at first keep pace, in spite of an adequate diet, cod liver oil and sunlight.

We know from animal experiments that the B and C factors can be absorbed from the organism, not only from the digestive tract but also when they are injected subcutaneously or intravenously. Whether the same applies to the fat-soluble A factor animal experiment has not yet been decided. A case recently reported by Blegvad, in which xerophthalmia occurred in a patient with cancer of the pancreas after occlusion of the bile duct, and in which the xerosis disappeared as a result of the subcutaneous injection of a concentrated cod liver oil preparation, indicates that the fat-soluble A factor can also be absorbed from the subcutaneous tissue. Blegvad employed a preparation of cod liver oil which Prof. E. Poulsen, Christiania, had prepared.

In five patients with xerophthalmia where there was imminent danger, I have given subcutaneous injections of cod liver oil in addition to the treatment I previously advocated. For this purpose I used ordinary cod liver oil which was sterilized in boiling water. It was previ-

ously sealed in glass tubes so as to prevent the access of air. For the first injection 0.5 c.c. was given, and then 1 c.c. daily for the first four to eight days.

Two of the patients were aged 6 months, one 1 year, one 2 years and 6 months, and one 4½ years. All of them had extensive xerosis of the conjunctivae and corneas; three also had corneal ulceration, one with perforation. They were all debilitated and backward in growth and vitality; catarrhal infections were present in all, pyuria in three, and two of them contracted measles.

All these patients recovered and their sight was preserved. Besides the cod liver oil injections, they had a diet rich in the fat-soluble A factor and also cod liver oil by mouth. I did not feel I could dispense with the treatment which had proved effective in my earlier cases. Nevertheless, I believe the cod liver oil injections were potent. The corneal ulceration undoubtedly became cleaner and healed more rapidly than it otherwise would have done, while the xerosis and the swelling and secretion of the conjunctiva disappeared sooner than I have observed in other similar patients.

These cases were not uncomplicated like that of Blegvad, where the patient only received the fat-soluble A factor by injection, but taken in conjunction with it they indicate that the fat-soluble A factor of the cod liver oil is absorbed from the subcutaneous tissue and rapidly passes into the organism.

The cod liver oil injections were painless, just like an oil of camphor injection, and there was no reaction at the site of inoculation for the first few days. After from four to eight days, a rather large infiltration always appeared, with redness and tenderness at the site of inoculation attended by indisposition and intermittent fever, the evening temperature being between 38 and 39 C. (100.4 and 102.2 F.). This lasted almost a week, but the tenderness persisted for several weeks afterward and the infiltration disappeared little by little. In none of the patients was there abscess formation.

In spite of these inconveniences, I consider the advantages are so great that we ought to give cod liver oil injections to every patient in whom the cornea is attacked. To insure against idiosyncrasy a small dose should be given first.

CONCLUSIONS

Deficiency in the fat-soluble factor is stated to be the cause of rickets and osteoporosis. I have previously shown that ordinary clinical rickets can hardly be due to the absence of the fat-soluble A factor,[5] and the majority of investigators who work with vitamins are now of the same opinion.

5. Bloch, C. E.: Der fettlösliche A. Stoff und die Rachitis, Monatschr. f. Kinderh. **25**:36 (March) 1923.

It is otherwise with osteoporosis. McCollum and his collaborators have found that young rats frequently develop osteoporosis when they are kept for a long time on a diet poor in the fat-soluble A factor.

By the usual clinical methods of investigation I have not been able to demonstrate osteoporosis in my patients with xerophthalmia, as mentioned in an earlier article. In the spring of the present year (1924) I tried whether such changes could be detected by roentgen-ray examination.

Five cases of xerophthalmia were investigated; two patients were aged 6 months, one aged 2½ years and one aged 4½ years, in addition to the before mentioned Case 2, but I did not succeed in demonstrating osteoporosis by this method; there was no striking diminution in calcium deposits or atrophy of the bones and only in one patient were there definite signs of rickets.

THE SIGNIFICANCE OF THE PRESENCE OF THE NEPHROGENIC ZONE OF THE KIDNEY IN THE NORMAL AND THE SYPHILITIC FETUS AND THE NEW-BORN *

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ROCHESTER, MINN.

The histopathology of the kidney in congenital syphilis is still in a state of confusion. Unacquainted with the histology of the new-born and of the fetus, many investigators are continually pointing out as abnormal that which is simply an expression of incomplete development.

The nephrogenic or neogenic zone of the kidney is a continuous layer of developing uriniferous tubules and glomeruli lying beneath the capsule. As each generation of tubules and glomeruli complete their development, the remains of the new-growing tubules are pushed toward the periphery of the kidney. This appositional growth is continued until the nephrogenic zone vanishes, and the development of the kidney is complete, so far as the formation of new elements is concerned. Further growth consists only of the enlargement of the tubules and glomeruli already present.

Authors have never been in agreement as to the exact time or the limits of variability when appositional growth of the kidney ceases, and the nephrogenic zone disappears. The present study was undertaken with the hope of definitely deciding this problem. Stoerk [1] asserts that it would be extremely important to know the exact time of the completion of kidney development, because such knowledge would be very helpful in making a diagnosis of congenital syphilis.

Campos [2] examined the kidneys of thirty-nine syphilitic premature infants at Johns Hopkins Hospital, and found the nephrogenic zone present in all. He also found that, of nineteen syphilitic infants born at term, all but two revealed this positive sign of retarded development. However, in eleven syphilitic infants, from 2 weeks to 5 months of age, the zone was absent. As controls he examined the kidney in forty-three normal infants, twenty of whom were premature and twenty-three

* Received for publication, Oct. 1, 1924.

* This work was done in the Department of Obstetrics and Pathology of the University of Minnesota, and in the Section on Pediatrics of the Mayo Clinic.

* Research partly supported by funds from the Children's Bureau, Department of Labor.

1. Stoerk, O.: Ueber Nierenveränderungen bei Lues congenita, Wien. klin. Wchnschr. **14**:958-964, 1901.

2. Campos, E. de S.: Pathological Changes in the Kidney in Congenital Syphilis, Bull. Johns Hopkins Hosp. **34**:253-262, 1923.

born at term. He concluded that the kidney is retarded in development in congenital syphilis, as the nephrogenic zone is present in the kidneys of syphilitic full term, stillborn infants, while it is absent in kidneys of normal, full term, stillborn infants. The value of his findings is impaired because he does not give the length and weight of the infants. Syphilitic infants are prone to be premature, and such data, therefore, are absolutely necessary. Also his control cases (forty-three) are inadequate to establish the normal time for the disappearance of the nephrogenic zone. It is difficult to understand how there can be retardation of development in practically every case, since no one pathologic change in cases of congenital syphilis is ever constant.

As early as 1874 Riedel [3] said that the formation of glomeruli in the zone of appositional growth was normally complete at the time of birth. In the same year Toldt [4] said that the formation of glomeruli could continue into the first days of extra-uterine life. Stroebe,[5] in 1891, was the first to recognize the relationship of congenital syphilis to renal development. He found the nephrogenic zone present in a supposedly mature stillborn infant with congenital syphilis, while in normal control preparations of the new-born, the zone was entirely lacking and subcapsular development always completed. However, he gave no data on the number of controls used, nor did he classify the infants as to length and weight. Hochsinger,[6] in 1898, in citing the cases of two stillborn infants, and three infants in the first week of life, did not assume a general growth arrest of the kidney because of syphilis, but only a segmentation of embryonal parenchyma of new formed connective tissue.

Hecker [7] believed that maceration in the kidney occurred later than in the liver and that for this reason this organ was more favorable for study. Besides, he thought the kidney was more regularly affected by the syphilitic virus than other organs. He was of the opinion that the structural development of the kidney was not complete at the time of birth, and that detection of the peripheral growth zone was not at all characteristic of syphilis. He believed that the nephrogenic zone decreased in width and intensity with the age of the fetus, but that no

3. Riedel: Quoted by Stroebe, footnote 5.

4. Toldt: Quoted by Stroebe, footnote 5.

5. Stroebe, H.: Zur Histologie der congenitalen Nieren- und Lungensyphilis, Centralbl. f. allg. Path. u. path. Anat. **2**:1009-1021, 1891.

6. Hochsinger, C.: Studien über die hereditäre Syphilis, Ed. 1, Leipzig, Deuticke, 1898, pp. 415-428.

7. Hecker, R.: Beiträge zur Histologie und Pathologie der congenitalen Syphilis sowie zur normalen Anatomie des Foetus und Neugeborenen, Deutsch. Arch. f. klin. Med. **61**:1-75, 1898; ibid. Neureres zur Pathologie der congenitalen Syphilis, Berl. klin. Wchnschr. **36**:1021, 1899; ibid. Neurere zur Pathologie der congenitalen Syphilis, Jahrb. f. Kinderh. **2**:375-384, 1900.

regularity could be recognized. He claimed to be able to demonstrate a marked zone in infants which he considered normal and "safely mature." On the other hand he had seen syphilitic premature infants in whom the zone was scarcely visible. In short, he believed that there was a noteworthy incomparability which plainly showed an individual variability of growth energy. He did not deny the possibility that in many cases retardation of growth can occur. Hecker's work comprises the examination of the kidney in 113 cases, of which twenty-five were syphilitic. His material was sufficient to have established fairly well the normal time for the disappearance of the zone and also its retardation, if any, in cases of congenital syphilis. However, he did not use the length and weight of the infants in the calculation of the probable age, and therefore, could not arrive at any definite conclusions.

Stoerk,[1] in 1901, after the study of the kidney in twenty syphilitic infants and in sixty controls in embryos, new-born infants and children, asserted that no nephrogenic zone should be found in the last month of intra-uterine life. He believed that only the outstanding changes of congenital syphilis were known, and not much regarding its effect on development. He maintained that the zone was not absent in any cases of congenital syphilis with definite histologic and anatomic changes; it was found in only two cases in which there was no suspicion of the disease. He said that the young malpighian corpuscles in their different stages of development can show manifold changes. He found such changes marked in postfetal kidneys of infants with congenital syphilis born at term with no abnormal relations of body length and weight. The oldest child with congenital syphilis was aged 3 months. He concluded that the toxin of syphilis causes a disturbance of normal development in the last fetal or first postfetal month of life. His work, however, is open to criticism in that he did not check the age of the infant by the body length and weight. The oldest child with a positive zone in the third month may not have reached the length of the full term infant, and so may have normally been entitled to a nephrogenic zone.

Herxheimer,[8] in 1908, wrote an excellent monograph on congenital syphilis. He did no original work as regards renal development, but his comprehensive bibliography is of great value.

Textbooks on embryology and pathology give a wrong conception of the nephrogenic zone. Kaufmann,[9] for example, thinks that the nephrogenic zone occurs in normal full term infants. Prentiss and

8. Herxheimer, G.: Zur pathologischen Anatomie der kongenitalen Syphilis, Ergeb. d. allg. Path. **12**:499-575, 1908.

9. Kaufmann, E.: Lehrbuch der pathologischen Anatomie für Studierende und Aerzte, Ed. 2, Berlin, De Gruyter, 1922, p. 1079.

Arey [10] assert that new renal corpuscles are formed peripherally from persisting nephrogenic tissue until the tenth day after birth. Such may be the case in certain animals, but as regards human beings it is incorrect. Aschoff [11] believes that the persistence of the nephrogenic zone cannot always be important, as it is found more or less plainly marked in all new-born infants. Keith [12] says that soon after birth the formation of new elements in the kidney ceases. Adami and Nichols [13] believe that in cases of syphilis a striking feature is the imperfectly developed kidney, and that immature glomeruli are to be seen in the cortex, apparently in many cases without proper communication with the secretory tubules. From this, the reader is led to believe that such a change is the rule rather than the exception.

I have studied microscopic sections of the kidney from 162 non-syphilitic fetuses and new-born infants. If there was any reason,

TABLE 1.—*Total Number (According to Length) of Normal and Syphilitic Infants. Figures 7 and 8 Contain Data from this Table*

	Normal Cases				Syphilitic Cases			
			Percentage				Percentage	
Length, Cm.	Total Number	No. with Zone Present	with Zone Present	No. with Zone Absent	Total Number	No. with Zone Present	with Zone Present	No. with Zone Absent
20 to 25	2	2	100	0	..	..	...	..
25 to 30	2	2	100	0	..	..	...	..
30 to 35	16	16	100	0	1	1	100	0
35 to 40	22	22	100	0	1	1	100	0
40 to 45	23	22	96	1	3	3	100	0
45 to 50	30	6	20	24	6	2	50	3
50 to 55	38	3	9	35	2	0	0	2
55 to 60	26	1	4	25	1	0	0	1
60 to 65	3	0	0	3	..	..	...	..
Total	162	74	...	88	14	8	...	6

however slight, for suspecting syphilis the case was excluded. Similarly I have studied the microscopic sections of the kidney in fourteen syphilitic fetuses and new-born infants. In all cases careful necropsies were performed and all organs weighed and studied microscopically. The crown-heel length and the weight were taken preceding each necropsy. The body length may be said to be the most accurate index of the age of the fetus or new-born child. The average body length in the full term infant is approximately 50 cm., and the normal variations may be considered as about from 48 to 52 cm.[14] All infants measuring less than

10. Prentiss, C. W., and Arey, L. B.: A Laboratory Manual and Textbook of Embryology, Ed. 3, Philadelphia, W. B. Saunders Co., 1922, 412 pp.

11. Aschoff, L.: Pathologische Anatomie, Leipzig, Barth, 1921, p. 500.

12. Keith, A.: Human Embryology and Morphology, London, 1921.

13. Adami, J. G., and Nichols, A. G.: The Principles of Pathology, Ed. 2, Philadelphia, Lea & Febiger, 1908-1909, p. 758.

14. Scammon, R. E., and Calkins, L. A.: Simple Empirical Formulae for Expressing the Lineal Growth of the Human Fetus, Proc. Soc. Exper. Biol. & Med. **20**:353-356, 1923.

TABLE 2.—*Total Number of Normal Infants (According to Weight). Figure 9 Contains Data from this Table*

Weight, Gm.	Total Number	Number with Zone Present	Percentage with Zone Present	Number with Zone Absent
0 to 500	8	8	100	0
500 to 1,000	20	20	100	0
1,000 to 1,500	28	28	100	0
1,500 to 2,000	21	12	57	9
2,000 to 2,500	10	2	20	8
2,500 to 3,000	13	3	23	10
3,000 to 3,500	23	0	0	23
3,500 to 4,000	25	1	4	24
4,000 to 4,500	4	0	0	4
4,500 to 5,000	4	0	0	4
5,000 to 6,000	4	0	0	4
Total	155	69	..	86

TABLE 3.—*Findings in Syphilitic Cases*

Case	Crown-heel Length, Cm.	Weight, Gm.	Nephrogenic Zone	Zone, Degree	Remarks
1	34.0	895	+	Marked	Death during delivery. Osteochondritis. Ascites. Pneumonia alba? Enlargement of liver, spleen and pancreas
2	38.0	1,220	+	Marked	Mother had two positive Wassermann tests during pregnancy. Stillbirth. Bleb formation and maceration of skin. Osteochondritis. Enlargement of liver and spleen
3	42.0	1,700	+	Moderate	Lived twelve hours. Osteochondritis. Bleb formation on skin. Enlargement of liver and spleen
4	42.0	1,800	+	Moderate	Stillbirth. Maceration and bleb formation on skin. Mother had positive Wassermann test during pregnancy. Osteochondritis. Enlargement of liver and spleen
5	43.5	?	+	Moderate	Stillbirth. Moderate maceration. Osteochondritis. Pemphigus syphiliticus. Enlargement of liver, spleen and pancreas
6	45.0	2,310	+	Marked	Lived twelve hours. Large macroscopic gumma of liver. Enlargement of liver, spleen and pancreas. Marked interstitial nephritis. DuBois abscess in thymus gland
7	45.5	2,425	+	Slight	Stillbirth. Slight maceration. Osteochondritis. Enlargement of liver and spleen
8	46.5	1,920	0	Definite	Lived three weeks. Malnutrition. Osteochondritis. Snuffles. Wassermann test on both mother and infant positive
9	47.0	2,920	+	Moderate	Stillbirth. Osteochondritis. Pemphigus syphiliticus. Enlargement of liver, spleen and pancreas
10	48.0	3,500	0	Definite	Lived eight weeks. Bronchopneumonia. Rhagades. Papules. Osteochondritis. Interstitial nephritis. Wassermann test positive. Enlargement of spleen. Improvement with antisyphilitic treatment
11	48.0	2,125	0	Definite	Stillbirth. Negro. Mother had positive Wassermann test during pregnancy. Maceration of skin. Osteochondritis. Rhagades at anus. Spleen enlarged
12	54.0	2,180	0	Definite	Lived two months. Emaciation. Both parents syphilitic with positive Wassermann tests. Infant had positive Wassermann test; lost weight
13	54.0	3,000	0	Indefinite	Stillbirth. Pemphigus syphiliticus of palms and soles. Wassermann test in mother positive. Enlargement of spleen
14	57.5	4,400	0	Definite	Lived six months. Mother syphilitic, had four stillbirths, and has one deformed child. Infant had positive Wassermann test. Died of acute bronchitis

Figure 1

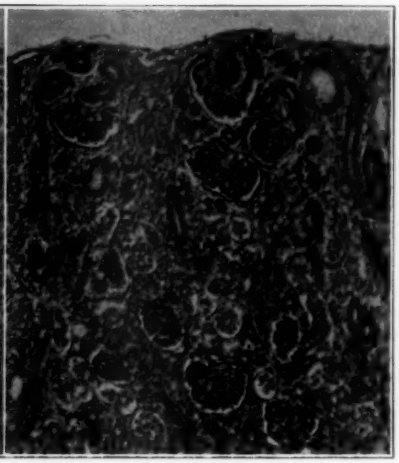

Figure 2

Fig. 1.—Marked nephrogenic zone in a premature infant, 38 cm. in length and 1,030 gm. in weight. The infant died (from exposure) a few minutes after birth. Necropsy negative.

Fig. 2.—Nephrogenic zone still present, but slight in an infant, 42 cm. in length and 1,570 gm. in weight. Infant died during induced labor. Necropsy negative.

Figure 3

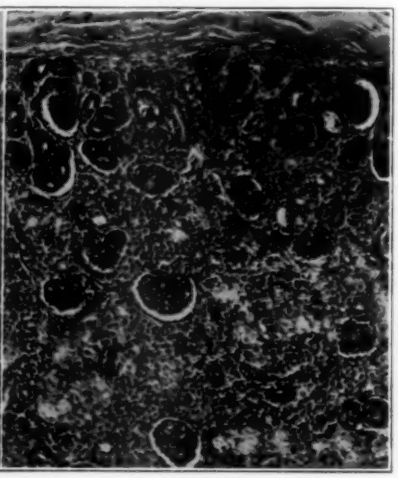

Figure 4

Fig. 3.—Nephrogenic zone definitely absent in slightly premature infant, 45 cm. in length and 1,610 gm. in weight. The infant died during delivery. Necropsy was negative except for slight laceration of the falx with hemorrhage and subpleural and subpericardial hemorrhages.

Fig. 4.—Nephrogenic zone present to a moderate degree in a syphilitic infant, 45 cm. in length and 2,310 gm. in weight. The infant lived for twelve hours. Necropsy revealed a large macroscopic gumma of the liver. The liver, spleen and pancreas were enlarged. On microscopic examination, a DuBois abscess was noted in the thymus, and marked perivascular round cell infiltration in the kidney.

48 cm. may be considered somewhat premature, and all those measuring more than 52 cm., somewhat postmature. The sex of the infant and the height of the parents are two of the important factors which produce variations. The menstrual age, as usually employed, is inaccurate and unscientific for pathologic studies. On the other hand the estimation of the age by the body weight is unreliable, as the weight is extremely variable. The weight of a dead infant after the length of 35 cm. has been reached, is approximately 219.3 gm. less than the weight of a living infant [15] (Figs. 1 to 6; Tables 1, 2 and 3).

It will be seen in Figure 7 that the curve representing the percentage of cases with the nephrogenic zone shows a sharp and marked drop at about the body length of 45 cm. Only five of 162 infants, in the control

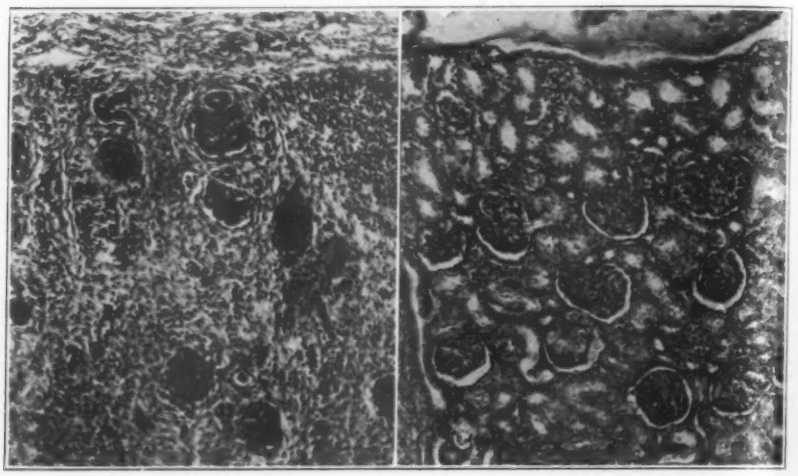

Figure 5 Figure 6

Fig. 5.—Nephrogenic zone present but slight, and also an area of subcapsular round cell infiltration in a syphilitic fetus, 47 cm. in length and 2,920 gm. in weight. Osteochondritis and pemphigus were present and the liver and spleen were enlarged.

Fig. 6.—Nephrogenic zone absent with glomeruli completely developed in a syphilitic infant, 46.5 cm. in length and 1,920 gm. in weight. The infant had snuffles and marked malnutrition. The Wassermann reaction was positive in both mother and infant. The infant lived for three weeks. Necropsy revealed osteochondritis.

series, with a length of over 48 cm., show the presence of the nephrogenic zone, and only one of these infants has a body length of more than 52 cm. In the smaller group of fourteen syphilitic cases, the percentage

15. Scammon, R. E., and Calkins, L. A.: The Relation Between Body Length and Body Weight in the Human Embryo and Fetus, Proc. Soc. Exper. Biol. & Med. **22**: 1924.

in which the nephrogenic zone was present shows a similar sharp and marked drop before the length of 48 cm. is reached. In none of the syphilitic cases was the zone present when the body length exceeded 47 cm.

Figure 8 shows in a different way that the development of the kidney tubules and the disappearance of the zone takes place prior to the arrival of the infant at full term (from 48 to 52 cm.). The number of

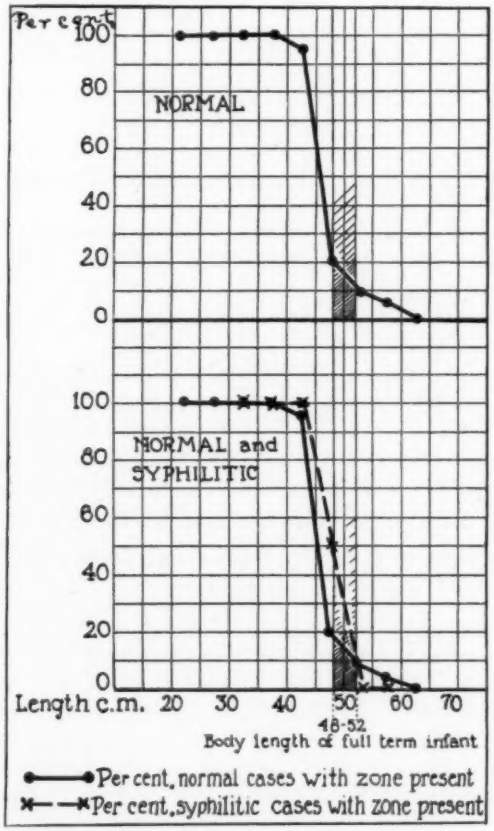

Fig. 7.—Nephrogenic zone disappeared in both normal and syphilitic cases prior to full term.

infants with the zone absent and the development complete approaches the total number of cases at the body length of between 45 and 48 cm.

The relation of body weight to the presence of the nephrogenic zone is not so striking, because weight is more variable with respect to age than is length. However, when taken together with the length, it becomes significant. The lowest body weight in which the nephrogenic zone was found absent occurred in an infant weighing 1,610 gm. Of

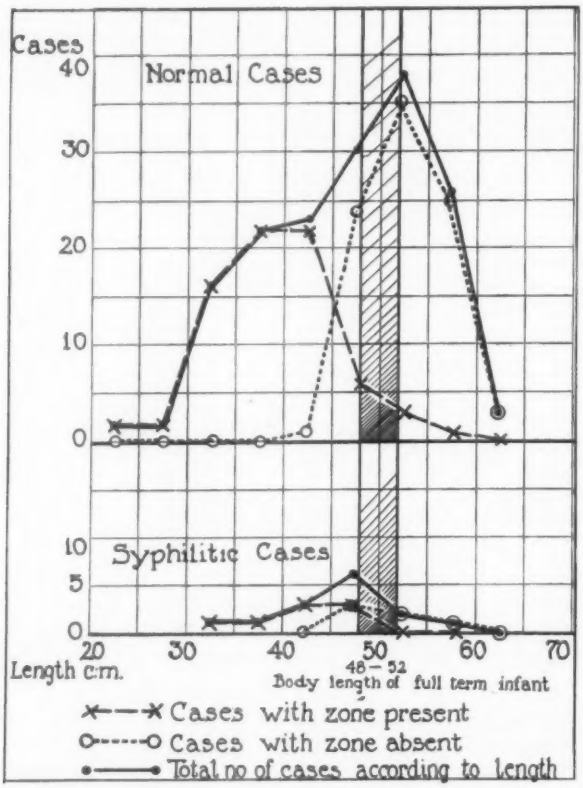

Fig. 8.—Development of kidney tubules and disappearance of nephrogenic zone prior to arrival of infant at full term.

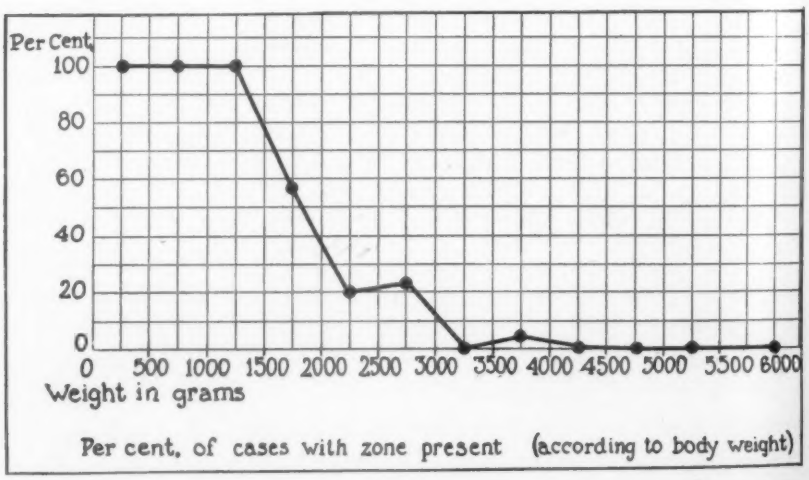

Fig. 9.—Percentage of cases with zone present (according to body weight).

the 155 cases in which the weight is recorded, only five show the zone to be present when the infant weighed over 2,500 gm. As seen in Figure 9, except for two cases with the zone present, in each of which the infants weighed 3,600 gm., the entire drop took place before the weight of 3,000 gm. was reached, while the maximal drop occurred before the weight of 2,000 gm. was reached.

COMMENT

The number of syphilitic cases in the series is small (fourteen); therefore, it cannot be stated positively that syphilis never causes a retardation of the development of the kidney and a continuation of the nephrogenic zone. However, it seems that such a retardation must be extremely unusual. It is probable that most of the infants reported as showing the presence of the neogenic zone with retardation of renal development in congenital syphilis were premature infants, and had not attained the body length of from 48 to 52 cm.

In a few of the syphilitic cases spirochetes have been found. However, in view of the definite clinical, serologic or pathologic findings of syphilis as shown in Table 3, an exhaustive search for the spirochetes was considered unnecessary.

CONCLUSIONS

1. The histologic study of the normal kidneys in 162 fetuses and new-born infants shows that the development of the renal tubules is completed when the infant is between 45 and 48 cm. in length.

2. At birth in the full term infant (from 48 to 52 cm.), the growth zone or nephrogenic zone of the kidney is absent.

3. The nephrogenic zone is usually absent when the weight of the dead infant is more than 2,500 gm.

4. The study of the kidneys in fourteen patients with congenital syphilis failed to show in a single instance a retardation in the development of the kidney with a persistent neogenic zone.

5. In congenital syphilis, the nephrogenic zone disappeared at the same time as it did in the control series, when the infant was between 45 and 48 cm. in length.

6. The presence of the neogenic zone is almost certain evidence of prematurity. Its prominence, whether slight, moderate, or marked, may give some idea of the age of the fetus.

ROENTGEN-RAY EXAMINATIONS IN DISEASES OF THE KIDNEY*

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Children between the ages of 5 and 15 years frequently have recurring attacks of abdominal pain, the cause for which it is difficult to determine. Pyelitis is common in infancy and childhood and the cure is sometimes hard to accomplish. In these two conditions roentgen-ray examinations are of great assistance in determining the presence or absence of a definite pathologic lesion in the kidney.

In recurring attacks of abdominal pain, diseases of the gastro-intestinal tract, enlarged mesenteric glands or lesions of the kidney must be considered carefully in every instance. The diseases of the gastro-intestinal tract which most frequently cause such attacks of pain are acute or subacute appendicitis, and congenital malformations. Acute appendicitis can be diagnosed usually by the physical signs, especially if accompanied by a leukocytosis. The congenital abnormalities give symptoms by producing temporary partial obstruction or chronic delay in emptying the intestine with constipation. A barium meal and enema will usually reveal this condition, and also will aid in excluding lesions of or about the appendix.

If the enlargement of the mesentery glands is acute, it is usually associated with infection in some other part of the body, most often the upper respiratory tract. If the lesions are chronic, the infection is due to tuberculosis, but may be associated with suppuration elsewhere in the body. Acute glandular enlargement is not difficult to diagnose. If the patient is seen early the glands may be confused with acute appendicitis or some other acute inflammatory process. Chronic mesenteric gland infection is very difficult to diagnose, and is frequently discovered only by roentgen-ray examination or operation. Sometimes the glands are palpated easily.

A third cause of repeated attacks of abdominal pain is some pathologic condition in the kidney, such as pyelitis, stone or a congenital malformation. In these conditions the attacks occur independently of the taking of food, and are not associated with indiscretions of diet. The attacks at first may be mild and come at infrequent intervals, or they may be severe and recur frequently. They may or may not be accompanied

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by nausea or vomiting. Fever is sometimes present, reaching 104 or 105 degrees, but it may be entirely absent. As a rule the children are perfectly well between attacks, and there is no interference with nutrition or with normal development. Their physical examination is usually negative. Occasionally there is some localized tenderness in the abdomen or in the flanks. There is rarely any spasm and no masses are felt. There is usually no indication for immediate surgical intervention. The white blood count may be elevated, but it is not infrequently normal. The urine may be normal, but usually contains a small or a considerable amount of pus in the sediment, and often a few red blood cells. A roentgenogram of the kidney with cystoscopy and pyelogram will help to indicate the nature of the pathologic process, if one exists.

Pyelitis is such a frequent disease in infants and young children and usually is of such a mild nature that it often does not receive serious consideration. Children often have this disease once or twice a year, either primary or due to infections elsewhere. The attacks may not be severe and may interfere very little with the child's general health or development. It is assumed that the attacks will eventually disappear without having done permanent damage to the kidney. Some clinicians believe that pyelitis in infancy or early childhood is a self limiting disease and not influenced greatly by any form of treatment. They are content with preventing constipation and forcing the children to drink more fluids and in trying to improve the child's general condition. Other physicians advocate a vigorous therapy with the injection of silver salts into the pelvis of the kidney. It is a question whether a complacent attitude toward these recurring kidney infections is justified. If a child has repeated attacks of pyelitis, or if any single attack is very severe or long continued, the advisability of a thorough investigation of the urinary tract should be considered.

The intimate connection between pyelitis and recurring attacks of abdominal pain is shown clearly by a study of a number of children made during the last year, and of a few others made some time ago. Stone in the kidney and congenital malformations are not uncommon. Tuberculosis also must be considered, although it is rare. It is most easily excluded as a cause of disease in the kidney by the application of the tuberculin test, and, provided there are not too many colon bacilli present, by the injection of the urine into a guinea-pig.

REPORT OF CASES

CASE 1.—R. LeB., aged 9½ years, entered the Children's Hospital Outpatient Department, Dec. 18, 1923. The family and past history were unimportant.

Present Illness.—At 3 months of age the patient began to have pain in the abdomen. This pain was intermittent in character, lasting sometimes a few hours and sometimes was present all day, occasionally accompanied by nausea. The child never had any vomiting. The pain stopped abruptly, sometimes without treatment, sometimes following an enema or castor oil. There were no

urinary symptoms and no blood in the urine was noted. During the first attack the temperature was 104 but since then there has been no fever.

Physical examination was entirely negative, except that the liver was palpable. There was no abdominal tenderness and no masses were felt. The tonsils were large and ragged, with a moderate enlargement of the anterior cervical glands.

Fig. 1 (Case 1).—C. G., stones in the kidney and marked dilatation of the ureters.

The urine contained a considerable amount of pus, but no blood. The patient was admitted to the hospital March 5, 1924. Bismuth series of the gastro-intestinal tract was normal. The roentgen-ray examination showed no stone in the kidney. Cystoscopy and pyelogram by Dr. Charles G. Mixter showed a normal pelvis and ureter on both sides. The tuberculin reaction was negative. Injection of the urine in a guinea-pig was negative for tuberculosis.

This child illustrates only one method of study in these children with recurring pyelitis and abdominal pain, and is presented here to show a normal pyelogram of the kidney. No pathologic condition in the kidney requiring surgical treatment was found.

CASE 2.—M. Z., a girl, aged 10 years and 2 months, was admitted to the Children's Hospital, Jan. 18, 1924. The family and past history were unimportant.

Present Illness.—For the last six years the patient has had attacks of abdominal pain accompanied by headache, vomiting, frequent micturition and slight rise in temperature. These attacks lasted from three to seven days and recurred five or six times a year. They were increasing in severity and in frequency.

Physical examination was negative, except for several bad teeth. The temperature ranged from 103 to 101. The white count varied from 8,000 to 10,000. The urine contained a large amount of pus.

Roentgen-ray bismuth series of the gastro-intestinal tract were negative. The tuberculin reaction was negative. Roentgenograms of the kidneys were negative for stone.

Cystoscopy and pyelogram by Dr. Mixter showed normal pelvis and ureter on both sides.

The child's bad teeth were removed. The urine became free from pus. In the two months since discharge from the hospital she has had no further attacks of abdominal pain and has gained 14 pounds (6 kg.).

The continuation of the pyelitis and the abdominal pain in this girl was due probably to the presence of a focus of infection in the mouth.

CASE 3.—O. T. S., was born Sept. 12, 1917, of normal labor. The child appeared normal at birth except for slight cyanosis. Physical examination revealed a congenital heart. The early history was unimportant.

When 2 years old the patient had a mild attack of pyelitis, and had several other attacks during the next year. The child was not very sick. The urine was not entirely free from pus, but never showed any blood.

One year after the first attack, when 3 years old, the child had an attack not unlike the others, except that the urine was blood tinged and the sediment contained a number of old red blood cells.

Physical examination showed no tenderness over the kidney or of the abdomen.

Roentgen-ray examination revealed a renal stone.

An operation was performed by Dr. Daniel F. Jones. Stone with the outline as indicated in the roentgenogram was removed from the left kidney.

Convalescence was normal. There were no more attacks of pyelitis.

CASE 4.—C. G., a boy, aged 7½ years, was admitted to the Children's Hospital Outpatient Department, Jan. 15, 1924. The family and past history were unimportant except that the patient had typhoid fever without complications at the age of 5 years.

Present Illness.—At 2½ years of age he began to have attacks of pain in the left upper quadrant of the abdomen, severe in character, lasting only for a few minutes at a time. The whole attack lasted two or three days, and recurred perhaps three times a year. After an attack the urine always contained pus which was present for several weeks or months, and sometimes clots of blood were found. Occasionally he had a temperature of 105 degrees during the attacks. Other attacks were afebrile. He never had any chills; occasionally he had vomiting. Between the attacks he was perfectly well. He was seen at the Children's Hospital Outpatient Department when 3 years of age, and a diagnosis of pyelitis was made.

The child was admitted to the hospital during one of the attacks, which lasted for an unusually long duration (two weeks), and was accompanied by a high temperature and a convulsion the day previous to admission.

Physical examination was entirely negative, except in the abdomen on deep palpation there was tenderness and spasm on the left side. Under ether, which was given for relief of the convulsion, his left kidney or at least a definite mass in this region was palpable, extending to the crest of the ileum. The white count was 27,000. The blood pressure was 135 systolic, 115 diastolic.

Fig. 2 (Case 2).—E. K., large hydronephrotic kidney and constriction of the ureter close to the pelvis.

In the hospital the blood pressure rose, the convulsions continued, and the abdominal tenderness increased. The nonprotein nitrogen of the blood was from 60 to 109. The urine contained a large amount of pus and a few red blood cells. Roentgen-ray examination showed stones in both kidneys.

Because of his serious condition an immediate operation was advised. On Jan. 19, 1924, Dr. Mixter exposed the left kidney. It was found to be three times the normal size and contained a number of areas of softening. These were opened with the escape of a large amount of pus and the evacuation of

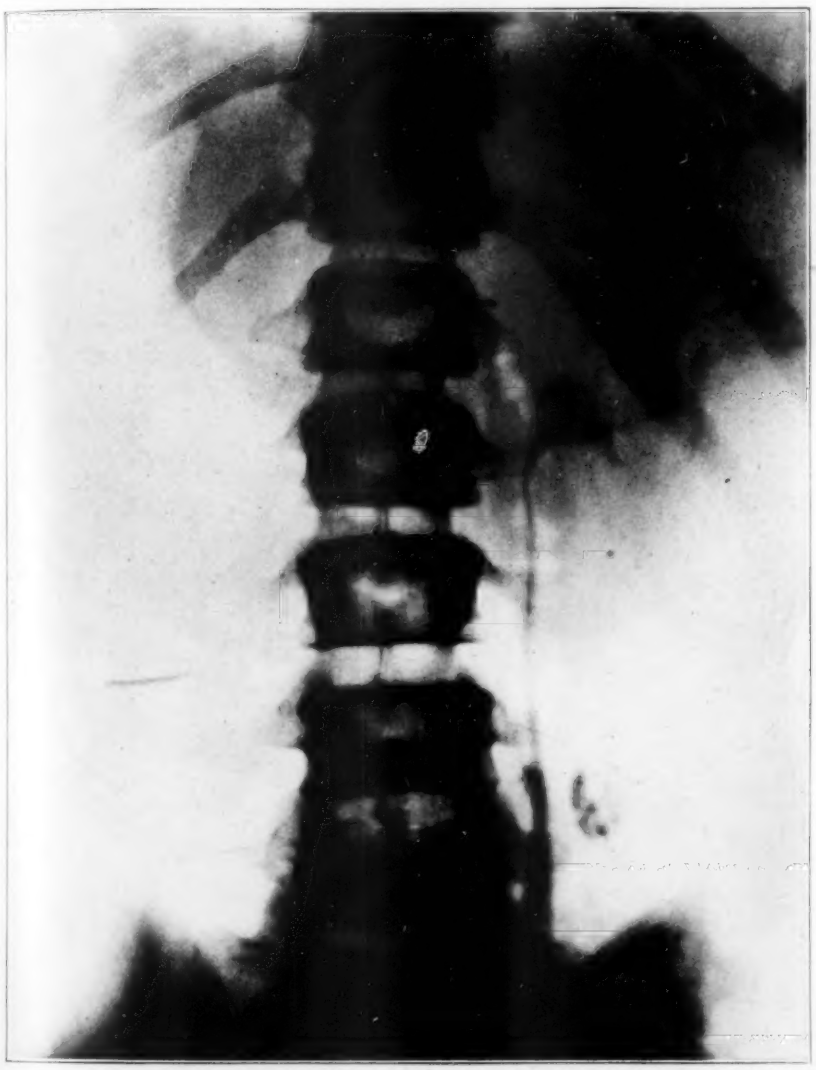

Fig. 3 (Case 3).—A. McG., incomplete filling of the kidney pelvis and calcified tuberculous gland outside ureter.

several stones. The kidney was drained, but not removed. The phenolphthalein renal function test on the other kidney was 10 per cent. in two hours and 15 per cent. in three hours. The patient made a good recovery from the operation. Five weeks after the operation, on February 27, Dr. Mixter did a cystoscopy and pyelogram which showed a stone in the left ureter which had not

been present previously, but apparently was dislodged at the time of operation. There was also a stone of considerable size in the left renal pelvis. The ureteral stone was removed March 17. The left ureter above the place where the stone was lodged showed marked enlargement. The stones in the right kidney are still present and will be removed later.

Fig. 4 (Case 4).—E. G., double pelvis and ureter.

It seems altogether likely that the stones in the left kidney at least were present at the time the diagnosis of pyelitis was made, four and one-half years before the operation. It is interesting to consider whether the infection of the kidney with the consequent destruction of kidney tissue and the resultant uremia could have been prevented by earlier operation.

Case 5.—E. K., a girl, born July, 1912, was one of twins. The family and past history were unimportant.

Present Illness.—In 1921, when 9 years old, the patient began to complain of pain in the abdomen. The first attack came without any warning and no cause was found. Since then she has had repeated attacks of pain associated with vomiting. These attacks come irregularly, one or two a week, or two or three weeks apart. Pain is always on the left side. The patient did not improve by dieting. There were no urinary symptoms.

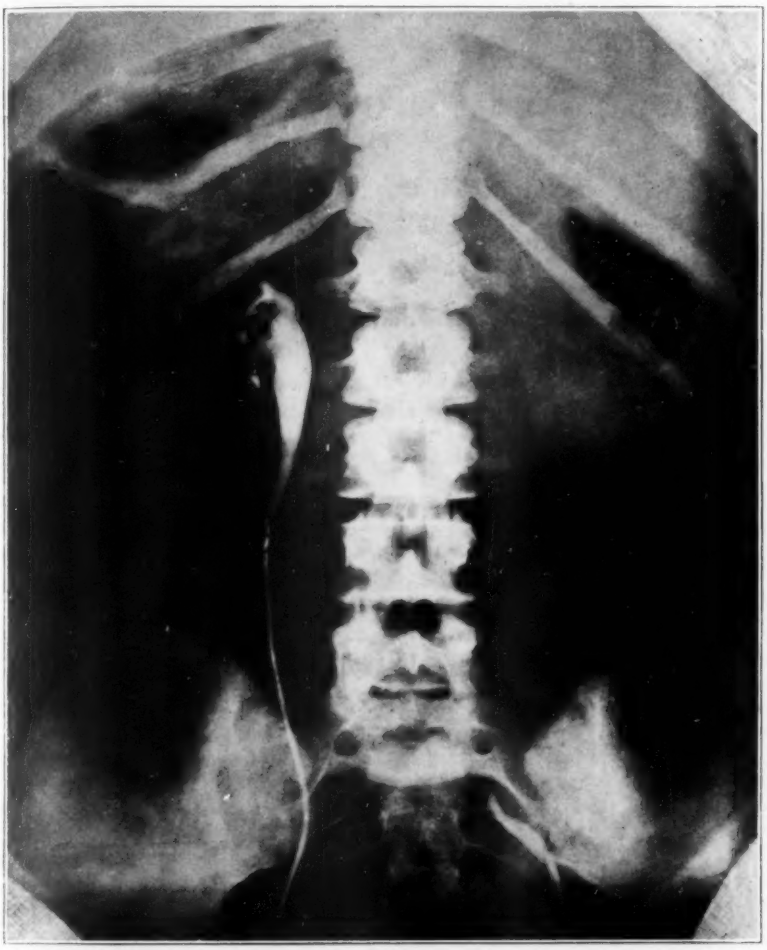

Fig. 5 (Case 5).—E. W., infantile kidney.

Physical examination, November, 1922, showed the patient to be in a good general condition. The abdomen was negative except on deep pressure it was possible to detect a little tenderness over the left kidney. The right kidney was easily palpable and not tender. The blood, urine and stool were normal.

Roentgenograms of the kidneys, ureter and bladder showed no evidence of a stone. The left kidney was slightly large.

Bismuth series of the gastro-intestinal tract was negative except for a little cecal and colonic stasis.

June, 1923, there was no improvement. The attacks were quite severe. On examination the right kidney was easily felt but left kidney was not felt. There was no tenderness.

The patient was admitted to the Children's Hospital, October, 1923.

Barium series of the gastro-intestinal tract were repeated and were normal.

Roentgenograms of the kidneys showed a normal right kidney, but it was impossible in several plates to see the outline of the left kidney. No stones were seen.

Cystoscopy and pyelogram by Dr. William E. Ladd showed that the right kidney was normal and a much enlarged left kidney pelvis hydronephrosis. In the roentgenogram there was a suggestive point of constriction in the left ureter just outside the kidney.

An operation was performed by Dr. Ladd, Oct. 24, 1923. Aberrant vessels, both artery and vein were found going to the lower pole of the left kidney and definitely constricting the ureter. These were ligated and cut. The kidney was much enlarged, sacculated and tense, with a thin wall. As soon as the vessels were cut, the tension was immediately relieved and the sacs collapsed. There was some apparently normal kidney tissue so that the kidney was not removed.

The patient had a normal convalescence. There have been no more attacks of pain, and the child is entirely well.

CASE 6.—A. G., aged 9 years and 10 months, was admitted to the Children's Hospital, March 10, 1924. The family and past history were unimportant except that a brother had tuberculosis several years ago, now healed.

Present Illness.—At 4 years the patient began to have attacks of abdominal pain and has had about twelve attacks since, usually associated with chills, not so severe as the one present on admission to hospital. That attack began one week previous to admission. There was pain in the back and flank in the region of the right kidney and in the right lower quadrant of the abdomen. The pain came in sharp intermittent spasms with a dull ache between. It radiated down the right leg and to the right heel. Five days previous to this attack the temperature was 103 degrees. There was nausea and vomiting. There have been no stools since. The urine was "greenish" in color, but not bloody.

Physical examination was negative except for moderate sized, cryptic tonsils with an enlargement of the cervical glands. Also in the abdomen in the right lower quadrant there was marked tenderness and slight spasm. There was much greater tenderness in the right flank and some tenderness of the dorsal spine. The white blood count was 16,000. The urine contained a large amount of pus. The tuberculin reaction was positive.

A roentgenogram was taken and showed what was believed to be a calculus in the ureter just above the sacro-iliac joint on the right.

On March 14, four days after admission, the temperature reached normal. A cystoscopy with pyelogram was done by Dr. Mixter. The examination showed nothing pathologic except that the right kidney pelvis was incompletely filled. The supposed calculus seen in the previous roentgenogram was outside the ureter and the shadow was caused by a calcified tuberculous gland. Phenolphthalein renal function test was impossible because of the blood in the urine following the cystoscopy.

On March 21, the pain was nearly gone. The white count was 10,000. The urine was still full of pus.

Bismuth series of the gastro-intestinal tract was normal.

On March 27, there was a return of pain. In the right upper quadrant of the abdomen a hard, tender mass was palpable, about the size of a hen's egg. There was moderate spasm in the right lower quadrant of the abdomen.

An operation was performed by Dr. Mixter. The abdomen was opened. The appendix was normal. The gallbladder was normal and there were no

adhesions. The incision was closed and the right kidney exposed. An aberrant vessel, an artery, was found running to the lower pole of the kidney. This was ligated and cut, and the incision closed.

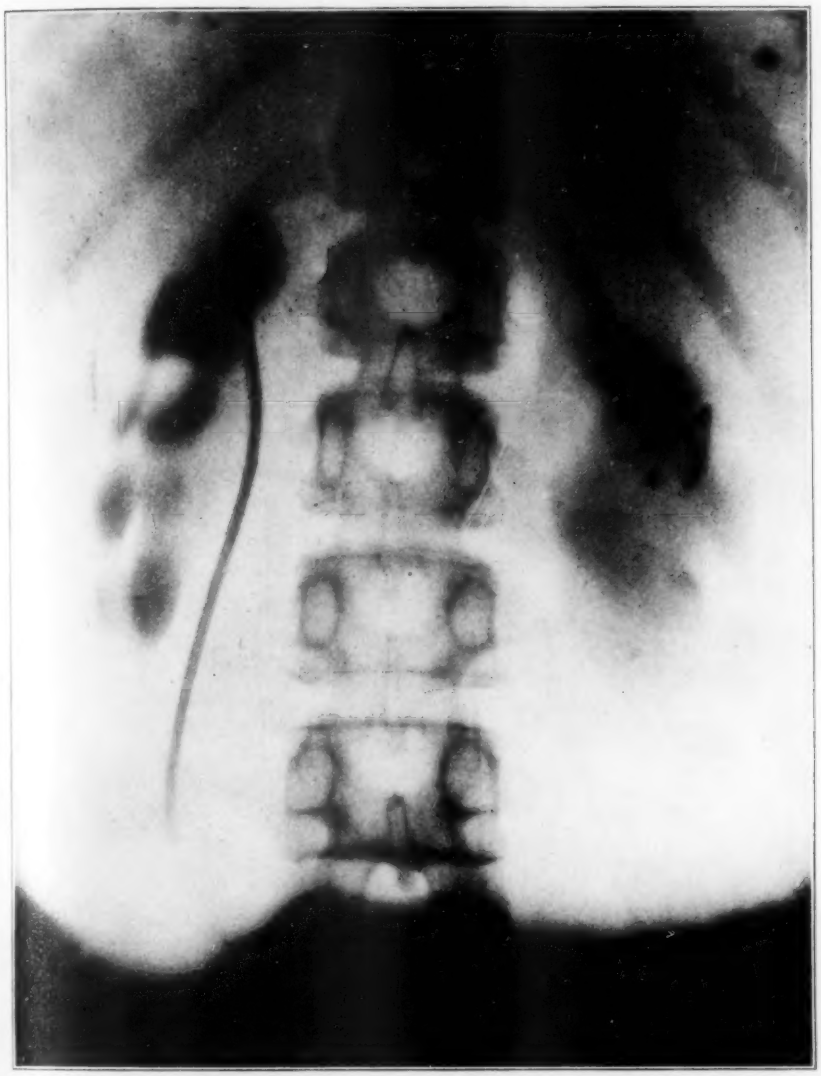

Fig. 6 (Case 6).—E. C., double hydronephrosis.

The convalescence was uneventful. There have been no more attacks of abdominal pain.

CASE 7.—E. G., a girl, born March 26, 1915. The family and past history were unimportant.

Present Illness.—In 1917, at the age of 2 years, the patient had an acute attack of abdominal pain with a temperature of 103. The attack was of very

short duration. There was no nausea and no other digestive symptoms. The physical examination was negative. The urine was normal. No satisfactory cause for the pain was found.

On Feb. 9, 1922, when nearly 7 years old, the child had a mild attack of pyelitis associated with a little head cold. She continued to have occasional

Fig. 7 (Case 7).—A. B., tortuous ureter with stone and dilated kidney pelvis.

attacks of abdominal pain and persistence of pus in the urine, sometimes in clumps, and occasional red blood cells. Because of the persistence of pus in the urine and the abdominal pain, her tonsils were removed March 30. There was considerable pus in the urine at the time, and the patient had a rather severe reaction following the operation. Associated with this she had an attack of

right sided abdominal pain which was believed to be due to acute appendicitis. She also had acute otitis media and bronchopneumonia. The urine did not clear after the operation.

On May 17, about six weeks after the operation, she passed one *Ascaris lumbricoides*. The child continued to have occasional attacks of indefinite discomfort in the upper part of the abdomen with nothing found on physical examination.

On July 6, four months after the tonsillectomy, an appendectomy was done by Dr. Beth Vincent. A very long and only slightly inflamed appendix with one definite adhesion was removed. The urine failed to remain clear, but never contained many pus cells. Some specimens were entirely normal, a few showed the slightest possible trace of albumin.

November 11, two months after the appendectomy, she had an attack of left sided abdominal pain with tenderness over the left kidney.

Roentgen-ray plates of the kidneys, ureters and bladder showed no evidence of stone. The kidneys were normal in size and in position. Attacks of abdominal pain continued increasing somewhat in severity, sometimes compelling her to assume a knee chest postion. They were, however, of short duration and as soon as they were over the patient was perfcetly well.

Nov. 16, 1923, cystoscopy and pyelogram were made by Dr. H. H. Crabtree. Normal except for the left kidney and ureter. This had a double pelvis and a double ureter for about one-half of its course. The two ureters were intertwined in their upper ends. The attacks of pain were undoubtedly due to temporary obstruction of the flow of urine from the kidney by the twisted ureters. Since the child's general condition is excellent and development normal, no operation on the ureters has been advised for the present.

Case 8. (Reported through the courtesy of Dr. Arthur H. Crosbie).—E. R. W., a girl, was born October, 1911. The family and past history were unimportant.

Present Illness.—At the age of 5 months the patient had pyelitis, which condition never entirely cleared up. The urine showed a considerable amount of pus and continued to do so until she was lost from observation three years later. Since then she has had more or less frequency and at various times has shown pus in her urine. The patient also has had more or less abdominal pain.

May 17, 1924, cystoscopy and pyelogram were made by Dr. Crosbie and showed an infantile kidney on the left side which was removed.

Case 9.—E. C., a girl, was born June, 1910. At the age of 4 years, and again at the age of 9 and at 9½ years she was seen in various Boston Hospitals, and had a diagnosis of pyelitis.

She was admitted to the Children's Hospital, January, 1921, suffering from an acute attack, with a high temperature and some pain in the flanks.

The physical examination was entirely negative.

The urine showed a considerable amount of pus and pure culture of an organism in the typhoid group which was not agglutinated by anti serums. There were no tubercle bacilli. Injection of the urine into a guinea-pig did not show tuberculosis.

The blood was normal.

Roentgen-ray examination failed to show any evidence of stone.

Cystoscopy and pyelogram were done Jan. 28, 1921, by Dr. Mixter, and showed that the base of the bladder was infected, and that both urethral orifices were patulous. Pyelogram showed enormous dilatation of both ureters and pelves with marked hydronephrosis.

Case 10.—M. D., a girl, born in 1920, was admitted to the Infant's Hospital at the age of 2 years with a diagnosis of pyelitis. The patient, when seen later at the Children's Hospital was still showing pus in the urine.

Cystoscopy and pyelography were done, Oct. 16, 1922, by Dr. Mixter. The bladder was reddened, and had a bleb-like appearance in the region of the trigon and right ureter. The right ureter was distended and edematous. There

Fig. 8 (Case 8).—M. J. C., kinking at the urethral pelvis junction on both sides, with slight dilatation of the ureters and slight dilatation of the pelves of the kidney.

was considerable difficulty in inserting a catheter at first because of a questionable obstruction about 2 inches (5 cm.) above the bladder. The left ureter was slightly edematous.

Injection of the urine into a guinea-pig showed no tubercle bacilli.

CASE 11.—C. K., born March, 1914, was admitted to the Children's Hospital in October, 1921, with acute illness of three days duration with a high temperature, and slight tenderness and distention of the abdomen, especially on the right side. There were no spasms and no masses. The white count was 18,000. The urine showed a large amount of pus.

Fig. 9 (Case 9).—C. K., ureters thickened and edematous, with considerable dilatation of the pelves.

Ten days later, when the temperature had reached normal a cystoscopy and pyelogram was done by Dr. Mixter, who found that both ureters were much thickened and dilated and that the pelves were larger than normal. On the right side the catheter made a complete figure of eight turn inside the ureter.

CASE 12.—M. J. C., a girl, was born Oct. 31, 1913. At the ages of 2 and 3 years she had "malarial attacks." In August, 1920, she had an acute febrile condition diagnosed as pyelitis, accompanied by some pain in the right flank. The urine never cleared, and at times contained a large amount of pus.

The patient was admitted to the Children's Hospital in July, 1922. The urine showed pus with pure culture of colon bacilli. No tubercle bacilli were found. Injection of the urine into a guinea-pig showed no tubercle bacilli.

A roentgenogram showed no stone.

Cystoscopy and pyelogram, July 5, done by Dr. Mixter showed kinking at the ureteral pelvic junction on both sides, with dilatation of the ureters and slight dilatation of the pelves of the kidney. In October of the same year, the left kidney and ureter were exposed and angulation in the ureter as shown by roentgenogram was found and another one, 1½ inches (3 cm.) below caused by a tight vessel overlying the ureter. This was cut. No aberrant vessel going to the kidney was found.

CASE 13.—A. B., a boy, was born in 1912. Ever since he began to walk he has had attacks of pain about once a month, localized for the most part in the left costovertebral region, colicy in character, associated with vomiting, but no fever. Sometimes blood was noted in the urine.

In 1921, when the patient was 9 years old, these attacks grew distinctly worse and he came to the Children's Hospital in an attack with a temperature of 104, spasm and tenderness all over the abdomen, most marked on the left side and especially in the left costovertebral space. The urine was clear. Pain subsided at the end of three days.

Cystoscopy and pyelogram were done by Dr. Mixter on March 12, 1921. The left ureteral orifice was not dilated. The catheter passed upward with considerable difficulty and then became obstructed owing to the presence of a stone which was revealed by roentgenogram, and which could be pushed by the catheter upward to a point opposite the third lumbar vertebra. The ureter was greatly dilated and tortuous with considerable dilatation of the kidney pelvis. The right pelvis was also moderately dilated and there was a definite kinking in its course with a right angle turn. No stone was found on that side.

March 25, an operation on the left side showed that the kidney cortex was thin, the ureter thickened and dilated to the size of a finger. There was no evidence of tuberculosis. No great amount of scar tissue. A stone the size of a large bean was removed.

COMMENT

These children had pyelitis early in infancy, and most of them were found subsequently to have either a stone in the kidney or some congenital kidney defect. They also had recurring attacks of abdominal pain associated with and dependent on pathologic kidneys.

The children with aberrant vessels are perhaps the most interesting because of the fact that aberrant vessels of the kidney are recognized as one of the not infrequent causes of abdominal pain, intermittent hydronephrosis or recurring attacks of pyelitis in adults. If aberrant vessels are frequent in adults, they must be equally common in children, and yet we find very little discussion of such conditions in pediatric literature. The aberrant vessel is usually single, either an artery or a vein, most often a vein, but both may be present, as in one of these patients. It is an extra vessel to the lower pole of the kidney and presses on the anterior surface of the ureter causing obstruction to the flow of

urine. As a rule, symptoms do not begin in the first few years of life. This is probably due to the fact that the symptoms do not occur unless the pressure is enough to cause obstruction. This is dependent entirely on the position of the kidney. If constriction of the ureter is sufficient, hydronephrosis will result and infection probably will follow. Almost invariably the urine of these children contains abnormal cellular elements, white blood cells in the majority of instances or occasionally red blood cells.

Children who have recurring attacks of pyelitis, or chronic pyelitis if it fails to yield to treatment, especially after the period of infancy, or who have recurring attacks of abdominal pain which are not explained adequately on some other basis, should have roentgen-ray studies made of the kidney including cystoscopy and pyelograms. Pyelograms should not be made indiscriminately, because it is a procedure requiring anesthesia and is sometimes followed by a considerable amount of discomfort, but in carefully selected persons, this method of investigation will reveal the true explanation of many otherwise obscure conditions.

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DUODENAL ULCER AND MELENA NEONATORUM*

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Comparatively few cases of melena neonatorum due to duodenal ulcer have been reported in the literature, and in these reports the descriptions of pathologic findings do not include graphic reproductions of the finer structures of the ulcers. The condition has been treated extensively in infants and children, especially by Helmholz,[1] whose findings indicate an infectious origin, and by Holt, who includes in his review of the literature nine cases observed in the first week of life. Wiederhofer[2] and Kundrat discuss the condition thoroughly. Two cases, with practically identical symptoms and pathologic findings, are reported here.

REPORT OF CASES

CASE 1.—The patient, a girl, born April 24, 1924, at 2:00 p. m., weighing 3,150 gm. The mother, aged 28, a primipara, had nausea, emesis and frequent headaches throughout pregnancy. For two or three weeks preceding delivery, she had had slight edema of the ankles. Labor lasted for sixteen hours and delivery was spontaneous. Breast feeding was begun twelve hours after birth, and was continued for twenty hours. The bleeding and clotting times were not taken.

The child cried lustily, nursed and appeared quite normal. At 5:00 p. m. of the second day there was a hemorrhage from the rectum, followed by a spell of cyanosis. Fibrinogen, whole blood and camphorated oil were given. The child died at 9:00 p. m. of the second day, thirty-seven hours after birth.

At necropsy, the child weighed 2,800 gm. and measured 51 cm. in crown-heel length. The skin and mucous membranes were very pale. The subcutaneous fat of the abdomen and chest was a light canary yellow. The thoracic viscera were extremely pale, but otherwise normal. The abdominal viscera, except those of the gastro-intestinal tract, were similarly anemic. The intestinal tract, from the pylorus to the rectum, was dark purple. The stomach was slightly distended with gas and contained blood-tinged mucus. The gastric mucosa was slightly congested in areas.

On the anterior wall of the duodenum, 1.5 cm. from the pyloric ring was an ulcer, measuring 6 by 4 mm., to the central part of which was attached a

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1. Helmholz, H. F.: The Relation of Duodenal Ulcers to Atrophic Conditions of Infants, Arch. Pediat. **25**:661-673, 1909; Ueber Duodenalgeschwüre bei der Pädatrophie, Deutsch. med. Wchnschr. **35**:534-539, 1909; Duodenal Ulcer in Infancy, Tr. Chicago Path. Soc. **8**:204, 1909-1911; Helmholz, H. F., and Gerdine, L.: Duodenal Ulcer in Infancy an Infectious Disease, AM. J. DIS. CHILD. **10**:397-409 (Dec.) 1915.

2. Wiederhofer, H.: Die Krankheiten des Magens und Darmes. In: Gerhardt's Handbuch der Kinderkrankheiten **4**:400, 1877-1883.

blood clot that filled the first portion of the duodenum. The remainder of the duodenum, the jejunum and the ileum were filled with clotted blood; the large intestine and rectum were distended with fluid blood.

The ulcer in the duodenum was sharply defined, with a smooth, even border and a depressed central portion (Fig. 1). After removal of the large blood clot from the duodenum, there still remained a small clot, about 1 mm. in diameter, which adhered tightly to the center of the ulcer.

The portion of the duodenum containing the ulcer was preserved, and serial sections were made from half of it. Under the microscope (low power magnification) the sharp borders of the ulcer, involving the mucosa and part of the submucosa, were seen (Fig. 2). There was a sudden transition from the nearly normal mucosa to the necrotic tissue which filled the ulcer crater. In the center of the necrotic area was a large thrombosed vein, which by serial sections was followed in one direction to the submucosa, where it became normal in size and devoid of the thrombus, and in the other direction to the surface of the ulcer where it opened freely. A zone of reaction, not marked, but definite, was noted in the submucosa, consisting chiefly of mononuclear cells, many of which showed acidophilic cytoplasm (Fig. 3).

Fig. 1.—Stomach and duodenum opened; ulcer at lower margin of duodenum.

In order to determine whether bacteria were present in the ulcer, several sections were stained with methylene blue, Gram's and Ziehl-Neelson stain. Careful examination did not reveal bacteria, except on the surface of the ulcer and the adjacent mucous membrane; these were mainly large rods and were judged to be ordinary saprophytes.

Case 2.—The patient, a girl, was born May 7, 1923, at 4:09 p. m. The mother was a primipara. Labor was comparatively short and not difficult. May 8, the bleeding time was three minutes, the coagulation time five minutes. On the same day the baby vomited a small amount of blood, and at 8:00 a. m. the amount vomited was considerable. At 9:30 a. m. there was marked bleeding from the rectum. At 11:00 a. m. a transfusion of 20 c.c. of whole blood from the mother was given. The child died at 3:00 a. m., May 9, thirty-five hours after birth.

Necropsy revealed that the infant was well developed and well nourished, measured 51 mm. in crown-heel length and weighed 3,225 gm. Pallor was marked. There was a hematoma (therapeutic) on the right subcostal ridge. A small amount of blood-tinged fluid was found in the peritoneal cavity, and there was a generalized staining of the peritoneum with hemolyzed blood. The heart weighed 18 gm., and except for marked paleness and slight reduction in consistency, was normal. The thymus weighed 12 gm., and was normal. The

thyroid weighed approximately 2 gm. The left lung weighed 20 gm. and the right 22 gm.; they appeared normal on the surface and on section. The spleen weighed 9 gm. and was normal. The liver weighed 140 gm., was very pale, and its consistency was greatly reduced. On section there was no darkening of the centers of the lobules. The gallbladder and ducts were normal.

The stomach contained a small amount of dark purplish-green material and a large amount of mucus, but no blood. From the pyloric ring to the

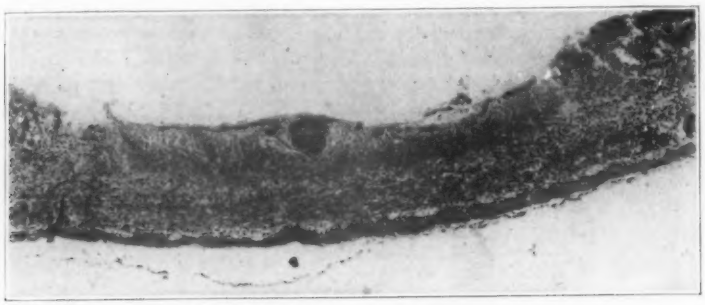

Fig. 2.—Low power magnification, showing the extent of ulcer; sharp margins; area of necrotic tissue and thrombosed vein.

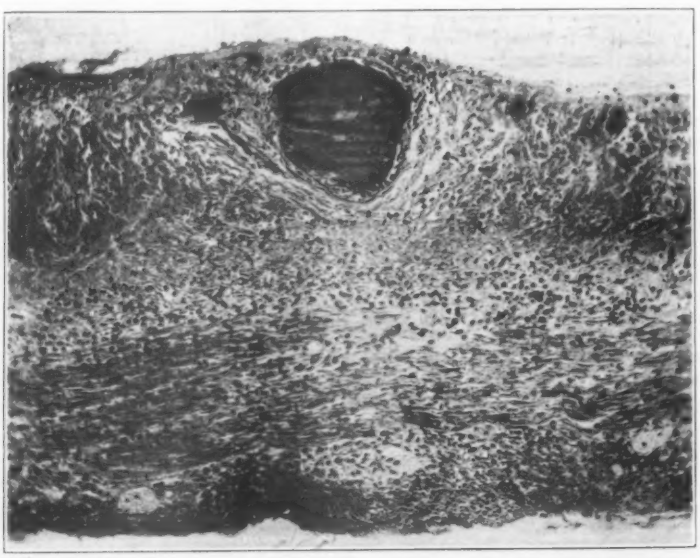

Fig. 3.—High power magnification of section through middle portion of Figure 1. Note the zone of reaction and infiltration of necrotic area.

anus there was a large amount of fluid and clotted blood mixed with meconium. There was no evidence of ulceration or any bleeding point in the gastrointestinal tract. The consistency of the pancreas was not increased. The suprarenal glands weighed 4.5 gm. each, and were apparently normal. The kidneys weighed 8 gm. each. They were pale and considerably reduced in consistency. There were a few uric acid infarcts. The head and cranial contents were normal.

Microscopic serial sections were made from the entire first portion of the duodenum, and in about the middle a definite ulcer was found. Under the microscope (low power magnification) (Fig. 4) the structure was seen to be almost identical with that of the ulcer in Case 1. The normal mucous membrane ceased at the margins, and the necrotic tissue of the ulcer crater began. The necrosis extended to the muscularis. In the center of the necrotic

Fig. 4.—Low power magnification, showing margins and depth of ulcer, and thrombosed veins in center of necrotic area, surmounted by a large amount of fibrin.

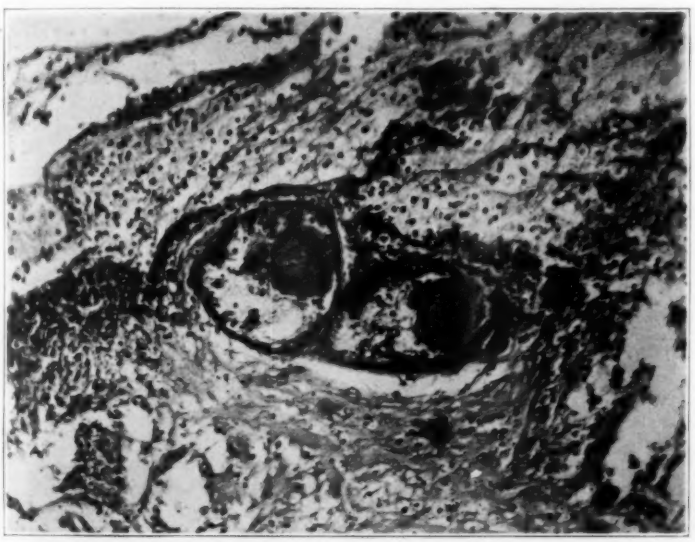

Fig. 5.—High power magnification, showing thrombosed veins in necrotic area, and fibrin, containing a large number of leukocytes.

area were two large thrombosed veins. As in Case 1, these were traced in section to the submucosa, where they became normal, and to the central point of the ulcer where they opened to the surface. A large amount of fibrin filled the ulcer crater and both this and the necrotic tissues, especially the former, were densely infiltrated with leukocytes (Fig. 5).

COMMENT

These cases are of interest because they show the striking similarity in the histologic structure of duodenal ulcers of new-born infants. With the histories almost parallel, the clinical condition and age at death nearly the same, they serve very well for comparison. As closely as can be judged, the bleeding had lasted for about the same length of time, and the pathologic changes appeared to be of the same duration in each.

Of great importance is the fact that in one patient (Case 2) the ulcer was entirely overlooked at necropsy, although the duodenum was examined especially for ulcer. This is the experience of most observers who have looked for lesions of the gastro-intestinal tract in cases of melena of new-born infants. Ander [3] mentions twenty-seven cases of melena, in only fifteen of which lesions were found; these were ulcerative changes in the stomach and duodenum.

It is noteworthy that a duodenal ulcer, not evident in a fresh specimen, may show clearly after the tissue has remained in fixing fluid for a few hours. The normal and abnormal mucous membranes are more sharply differentiated by the fixing process.

It is not surprising that such ulcers have not been detected in a higher percentage of cases. A very small ulcer, extending only 1 mm. or less below the surface of the mucosa, might easily be overlooked. A fold in the mucous membrane involving the ulcer, or a thin film of blood or mucus, could obscure it, or the change in the mucous membrane may not be so far advanced as to make the pathologic area evident macroscopically. Helmholz [1] has described a patient with a history very similar to that in Cases 1 and 2. At necropsy the duodenum was apparently negative, but a microscopic examination revealed necrosis of the mucosa, marked hemorrhage, and polymorphonuclear infiltration in the submucosa. In reporting this case Helmholz urged that more attention be given to the microscopic study of melena, a condition so often said to be characterized by the absence of macroscopic lesions. In the absence of such lesions, it has been assumed that the bleeding is due to oozing from the mucous membrane of the gastro-intestinal tract, following a hyperemia which results usually from faulty establishment of the pulmonary circulation. This hyperemia is not found at necropsy, because, it is said, the vascular system has been depleted by the hemorrhage for which the hyperemia is responsible. However, it is improbable that such rapid and extensive hemorrhage is due to oozing.

Several writers have reported cases of melena which they ascribe to a variety of causes, such as hyperemia of the lower esophagus (Chrza-

3. Ander, quoted by Neumann, H.: Arch. f. Kinderh. **12**:54, 1891.

nowski [4]), changes in the gland epithelium of the stomach and duodenum, with dilated vessels (Lövegren [5]), and pyemic disease (Kundrat-Wiederhofer). Certain observers still believe that cases of melena should be included in the general category of conditions referred to as "hemorrhagic disease of the new-born infant." No doubt there are infants whose bleeding and coagulation times are increased, and some of these bleed from the mucous membranes, umbilicus and other parts of the body. However, according to some of the more recent reports on the disease, many errors of diagnosis have occurred, owing to too great a readiness to call any and every case in which there is bleeding hemorrhagic disease of the new-born infant. More extensive and careful pathologic examinations have greatly reduced the number of cases which may rightly be included under this term. Case 2 serves to emphasize this fact. With a normal bleeding and clotting time, the infant bled to death on the second day of life. The clinical diagnosis was hemorrhagic disease in spite of the blood findings. After the ulcer was demonstrated the diagnosis was, of course, changed. Unfortunately the clotting and bleeding times in Case 1 are not known.

In the light of these findings, as of those reported by Helmholz,[1] it would appear that by more careful search of the gastro-intestinal tract, a much larger number of ulcers will be found, mascroscopically as well as microscopically, in explanation of melena of the new-born infant.

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AN EXPERIMENTAL STUDY OF THERAPEUTIC PROCEDURE IN PYELOCYSTITIS*

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The therapeutic results in the treatment of pyelocystitis are still far from satisfactory. Alkalinization of the urine is usually effective in the treatment of infections of the urinary tract of infants and children, although its mode of action is still practically unknown. In an attempt to throw some light on this question, the first three of the following studies were undertaken.

1. THE USE OF ALKALIS IN INFECTIONS OF THE BLADDER IN RABBITS

Sterile urine was obtained by catheterization from eleven rabbits, weighing from 900 to 1,200 gm. The rabbits were then placed on a diet consisting of oats and bread with a small amount of cabbage or lettuce until the urine became strongly acid. After a week the entire series was injected intracystically with 10 c.c. of a mixture containing equal amounts of 5 per cent. starch solution and a twenty-four hour culture of colon bacilli in dextrose brain broth. Five days later the

TABLE 1.—*The Average Daily Output of Urine for Twenty-Four Hours During Infection*

Rabbit	Cubic Centimeters	Days of Infection
420	82	60
424	110	13
419	45	20
Average	79	

infection was found to be established. Five rabbits were then given 0.5 gm. of sodium bicarbonate twice a day, at 9 a. m. and at 5 p. m. The urine became alkaline after one day in each instance. Sodium citrate in the same dosage had been tried in an earlier experiment, but as four animals had died, it was not used further. Unfortunately, two of the five rabbits died from intercurrent infection of the lung and pericardium shortly after the initiation of the experiment, so that but three rabbits were available for study (Table 1).

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* From the Section on Pediatrics, Mayo Clinic.

The six control rabbits remained on the acid diet and the urine was tested daily. Three, however, failed to develop a very definite infection of the urinary tract, for the number of bacteria in the cultured urine was always low. All of the six lived long enough to make possible the determination of an average daily secretion (Table 2).

The experiments show that the use of alkalis definitely increases the output of urine, and may have some effect on the diminution of the bladder infection. The control rabbit, which had a urinary output as

TABLE 2.—*The Average Daily Output of Urine for Twenty-Four Hours During Infection*

Rabbit	Cubic Centimeters	Days of Infection	Remarks
418*	92	100	Still living, urine positive for colon bacillus
417	42	40	Chloroformed
415	19	30	Chloroformed, urine negative for colon bacillus
416	13	?	Colon bacillus present only once on culture; 200 for each cubic centimeters
421	29	?	Colon bacillus in small numbers on three occasions
422	21	0	Urinary cultures all negative
Average	25		

* Rabbit 418 was under observation for a considerable period, and was found to consume usually about three times as much water as any of the other rabbits which we have controlled as to intake and output, so that we believe it is only fair to exclude this animal from the series when making our average. Including Rabbit 418, the average would be 36 c.c.

large as any of the rabbits receiving alkalis, still had cystitis after three months, showing that a large urinary output is only one of a number of factors in the clearing up of infection in the urinary tract.

2. THE PYROGENETIC ACTION OF THE FILTRATES OF OF COLON BACILLI

The effectiveness of the alkalis in clearing up symptoms and lowering the temperature of patients, without of necessity producing any special changes in the urine, led us to examine the pyrogenetic action of the filtrates of colon bacilli cultures when grown in acid and alkaline broths. Eight rabbits were used in each of the two series of experiments. The temperature of all animals was taken for twenty-four hours before starting the experiments, and one, two and five hours after the injection of the cultures.

In the first series of experiments 3 c.c. of broth and of the broth culture were used. The control animal given the alkaline broth reacted with a rise of 3.9 and 1.9 degrees in temperature; those receiving the acid broth had a rise of 2.0 and 1.5 degrees. The animal receiving the acid broth filtrate had a preliminary rise of 0.3 and 0.5 degrees, followed by a sharp secondary drop of 3.6 and 4.9. One rabbit, receiving acid broth filtrate, died six hours after injection. The alkaline broth filtrate produced in one animal a preliminary rise in temperature of 1.7

and then a fall of 4.4. In another, there was a gradual drop of 2.4. The first of these animals died the day following the inoculation. The reactions are illustrated in Figures 1 and 2.

This series of experiments, as mentioned briefly in a former communication,[1] shows practically no difference in reactions of animals to acid or alkaline broth filtrates. The over-stimulation of the heat center,

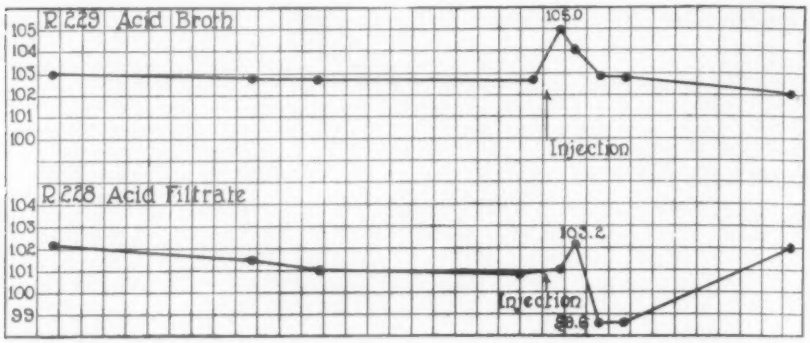


Fig. 1.—Febrile reaction after injection of acid broth and filtrate.

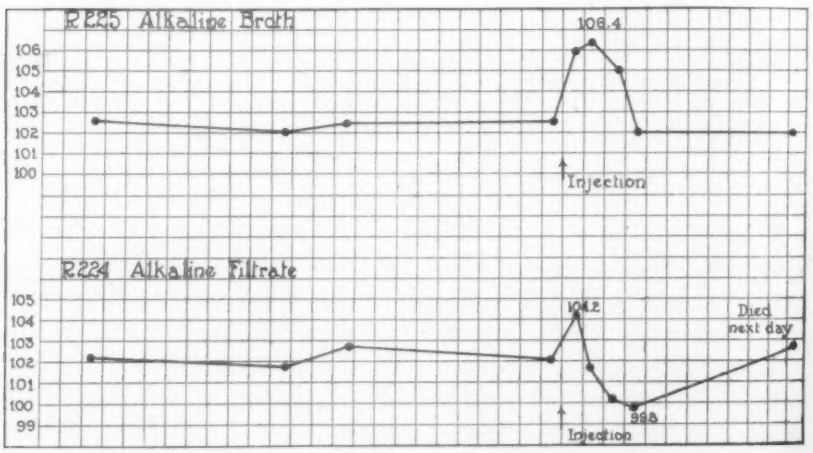


Fig. 2.—Febrile reaction after injection of alkaline broth and filtrate.

as manifested by a drop rather than by a rise in temperature, made us repeat the experiment, using only 2 c.c. of material instead of 3 c.c.

The results of the second series of experiments with 2 c.c. injections tally well with those in which 3 c.c. was injected. The acid broth filtrate injections produced high fever in both animals, and the alkaline broth

1. Helmholz, Henry F.: Drug Therapy in Pyelitis, J. A. M. A. **79**:285-286 (July 22) 1922.

filtrate in one instance caused a preliminary rise in temperature and then a slight drop. The animal died six hours after injection. The second animal exhibited a preliminary drop of 2 degrees and then a moderate rise.

In the experiments with 3 c.c. injections, there is no choice between the acid or alkaline broth filtrate in the severity of reaction produced. If subnormal temperature is taken as a criterion of severity of reaction, then the alkaline broth filtrate is definitely more toxic than a similar acid filtrate.

A series of twenty-four experiments was performed, comparing the pyrogenetic effects of colon cultures grown in sugar-free and sugar-containing broth. Two sets of experiments were performed, using 2 c.c. of broth intravenously, and one set using 3 c.c. of broth. The reaction of the filtrate injection was always definitely more marked than that of a similar amount of the culture medium, but there was no constant and essential difference in the reactions following the injections of the filtrates from organisms grown in sugar-free broth and those in bouillon containing sugar.

3. THE EFFECT OF CHANGE OF REACTION OF THE MEDIUM ON THE GROWTH OF THE COLON BACILLUS

It has been asserted repeatedly by observers that when a pyelocystitis does not clear up under alkaline treatment or with the administration of urotropin, it often happens that if one changes from alkalinization of the urine to urotropin and acidulation, and then back again, the pyelocystitis may clear up. The good results are ascribed to the rapid change in the reaction of the urine.

A series of experiments, to determine the effect of rapid change of reaction on the growth of the colon bacillus, soon revealed that the growth of the colon bacillus tended to make alkaline mediums acid and acid mediums more acid in the presence of sugar; in sugar-free broth the acid mediums became alkaline, and the alkaline mediums more alkaline when *Bacillus coli* was grown in them.

The work of Chesney [2] and others has shown that there is a lag in the growth of all bacterial cultures that are more than four hours old. He divided the life cycle of bacterial cultures into four phases: (1) latent period, four hours; (2) period of maximal rate of growth, five hours, fifth to ninth hour; (3) stationary period, three hours, tenth to twelfth hour, and (4) period of decline, after twelfth hour. It is, therefore, necessary in any lag experiments to use cultures that are between five and nine hours old in order to avoid the lag due to the age of the culture. In all of the experiments cultures that were between

2. Chesney, A. M.: The Latent Period in the Growth of Bacteria, J. Exper. Med. **24**:387-418 (Oct.) 1916.

four and nine hours old were used. All experiments were performed in duplicate and the average counts taken.

Without going into the details of the experiments, which will be reported elsewhere, the outstanding feature was the very marked inhibition of growth of the colon bacillus when transferred from alkaline (hydrogen-ion concentration 8.4) to acid mediums (hydrogen-ion concentration 5.2) (Fig. 3), and that there was no effect when transferred from acid to alkaline mediums; in fact the growth was usually more rapid than that of the control.

It would seem that the change from acid to alkaline reaction is beneficial to the growth of the organism, and that the transfer from

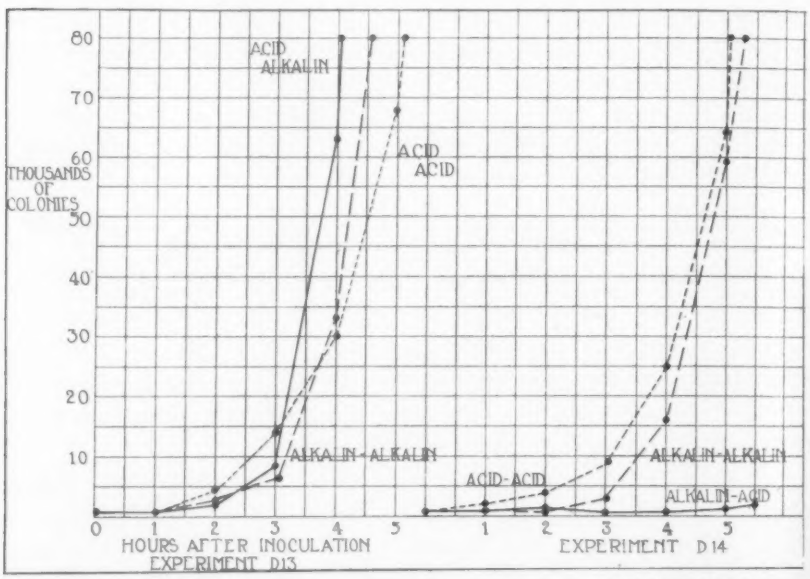


Fig. 3.—Rapidity of growth after transfer to mediums of different hydrogen-ion concentration.

alkaline to acid reaction definitely retards the growth of the colon bacillus. Whether or not the benefit of the treatment by rapid change of reaction is due to this inhibiting effect on growth cannot now be determined, but it furnishes a lead which should be followed experimentally.

4. THE USE OF ACRIFLAVIN

Recently Davis[3] has reported very excellent results from treating urinary infection in the rabbit with acriflavin. This substance acts best

3. Davis, E. G., and Beck, G. H.: Urinary Antisepsis: the Secretion of Antiseptic Urine by Man Following the Oral Administration of Proflavine and Acriflavine: Preliminary Report, J. Urol. **5**:215-233 (March) 1921.

on alkaline urine, so that it seemed an ideal drug to combine with the alkalis in the treatment of pyelitis of infants and children. We used it in three children without the slightest effect on the infection. In each instance the dose was increased up to a point at which gastro-intestinal symptoms, such as vomiting or diarrhea, or both, were produced. In all three cases, with the maximal dosage, there were innumerable bacilli in 0.5 c.c. of urine. Although the number of experiments is too small to warrant definite conclusions, it can be said that with an alkaline urine, the largest tolerated dose of acriflavin did not produce satisfactory results.

REPORT OF CASES

CASE 1.—A girl, aged 4 years, weighing 37 pounds (16.8 kg.) had had infection of the urinary tract with colon bacillus since she was 8 months of age. She had been treated with alkalis, and later with urotropin, but the only way in which the urine could be made acid was by administration of sodium acid phosphate, and, therefore, acriflavin, 0.025 gm. every eight hours, three times a day, was given. The urine became definitely yellow after two days, but innumerable colon bacilli were found on culture. Five days later, culture still showed innumerable bacilli. The dosage was increased to 0.05 gm. twice a day, and 0.025 gm. once a day. The urine became very yellow, but four days later a large number of colon bacilli were found in 0.5 c.c. of urine on culture. The dosage was then increased to 0.05 gm. three times a day, and three days later culture demonstrated innumerable colon bacilli in 0.5 c.c. of urine. The child vomited several times after medication, and the bowels were loose for a few days. Discoloration of the mouth, and of the skin around the rectum became noticeable.

CASE 2.—A baby girl, aged 7 months, had developed pyelitis two days after birth. Her weight at birth was 5 pounds (2.3 kg.). The first urinary culture disclosed staphylococci only. Later staphylococci and colon bacilli were found, and later still, only colon bacilli. Alkaline treatment, and urotropin given in doses as high as 10 gr. four times a day, brought no results. Then acriflavin was given in doses of 0.01 gm. every eight hours, three times a day. Sodium citrate and sodium bicarbonate, 0.5 gm. four times a day, were also given. Two days later innumerable colon bacilli were found on culture in 0.5 c.c. of urine. The urine was cloudy with pus. Five days after starting the treatment, it was necessary to discontinue the acriflavin because the stools became diarrheal. The dosage was reduced to 0.005 gm. three times a day, and the urinary cultures showed innumerable colon bacilli in 0.5 c.c. of urine. The dosage was gradually increased, but on reaching 0.01 gm. three times a day, a condition of diarrhea was again produced. There was absolutely no effect on the number of bacteria in the urine, which was definitely alkaline.

CASE 3.—A boy, aged 7 years, with bilateral dislocation of the hips, spina bifida, and mild hydrocephalus, was examined, and pyelitis, which had probably been present for a number of years, was found. Acriflavin in doses of 0.05 gm. every eight hours, three times in twenty-four hours, was given, besides 20 gr. of sodium bicarbonate four times a day. Two doses were taken without difficulty, but the third was vomited. However, another dose was given. After twenty-four hours the urine was strongly colored and alkaline. On culture, innumerable organisms were found in 0.5 c.c. of urine. The dose was reduced to 0.025 gm. for twenty-four hours, and then returned to 0.05 gm. three times a day. Two days later severe diarrhea with yellow stools developed. The urine was a dark, greenish-yellow color, alkaline, and contained pus 4 with innumerable colon bacilli in 0.5 c.c.

5. THE USE OF UROTROPIN

The interesting studies of Shohl and Deming,[4] and Shohl and Janney,[5] and our inability to make headway in clearing up chronic infections of the urinary tract in children, induced us again to take up the use of urotropin in the treatment of pyelitis. In looking back, it is not surprising that we did not obtain better results; first, because the dosage was unquestionably relatively low, and second, because the reaction of the urine was not sufficiently controlled. In the course of our work we were surprised at the favorable results we obtained, since, according to the work of other observers, we should not have had favorable results. Burnam,[6] Hinman,[7] Shohl and Deming, and many other observers in this field, have insisted that formaldehyd in the urine in concentration of at least 1 : 20,000 or 1 : 30,000 is necessary to obtain good results.

We started treatment with a particularly unfavorable case, a boy whose pyelitis had lasted for at least six years, and was complicated by cord bladder and posterior urethral stricture. On one occasion, after instrumentation, there was complete suppression, and it was necessary to perform suprapubic cystotomy. One year before we had tried various modes of treatment without the slightest effect on the pyuria. On this visit we prescribed 2.5 liters of water a day for a period of four days, but no change in the pyuria resulted. We then added 1 gm. of urotropin every six hours, increasing the dose to 1.5 gm. four times a day after a short interval. In the course of eleven days the urine was sterile, and at no examination did we find the formaldehyd in greater concentration than 1 : 100,000, and that only very occasionally. We have had reports from the boy at intervals of six months, and his urine has been constantly free from pus.

The foregoing excellent result led us to try urotropin in a number of other chronic cases, seventeen in all. In ten cases the condition was cleared up completely, and in only one of the remaining seven was failure definite. The details of the ten cases may be noted in Table 3. In the other cases, it was impossible to carry out the treatment under control because the patients were unable to remain for observation. However, we attempted to carry out the treatment under the direction

4. Shohl, A. T., and Deming, C. L.: Hexamethylenamin: Its Quantitative Factors in Therapy, J. Urol. **4**:419-437 (Oct.) 1920.

5. Shohl, A. T., and Janney, J. H.: The Growth of *Bacillus coli* in Urine at Varying Hydrogen-Ion Concentrations, J. Urol. **1**:211-229 (April) 1917.

6. Burnam, Curtis F.: An Experimental Investigation of the Value of Hexamethylenamin and Allied Compounds, Arch. Int. Med. **10**:324-334 (Oct.) 1912.

7. Hinman, F.: An Experimental Study of the Antiseptic Value of the Internal Use of Hexamethylenamin, with the Report of a Simple Clinical Method of Quantitative Estimation of Formaldehyd, Tr. Am. A. Gen.-Urin. Surg. **8**:235-269, 1913.

TABLE 3.—*Patients Successfully Treated with Urotropin*

Case	Sex*	Age	Duration of Symptoms	Infecting Organism	Date	Organisms in 0.5 c.c. Urine	Urotropin Four Times Daily, Gm.	Hydrogen-ion Concentration, Urine	Concentration of Formaldehyd in Urine	Pus, Scale 0 to 4	Remarks
1. F. H	♂	11	6 yr.	Bacillus coli.....	7/16/22	Innumerable	0	6.2	None	4	Posterior urethral stricture; dribbling since birth; first acute attack when five years old; 2,500 c.c. water from 7/16 on
					7/18/22	Innumerable	1.0	6.8	None		
					7/22/22	110	1.0	6.8	None		
					7/25/22	...	1.5				
					7/27/22	None	1.5	6.8			
					8/ 4/22	None	1.5	6.2	1:20,000		
					8/11/22	3	0	6.8	None		
					8/19/22	10	0	5.8	None		
2. F. M.	♀	11	4 yr.	Bacillus coli.....	4/21/22	Innumerable	0	...	....	1	Four years' duration; ureteral catheterization showed bilateral involvement of kidneys; sodium acid phosphate 1.34 gm. four times a day
					4/26/22	Innumerable	1.0	6.6	None	1	
					4/29/22	None	1.0	7.4	None	1	
					5/ 2/22	None	0	0	None	1	
3. C. B.	♂	12	1 mo.	Staphylococcus aureus	4/11/22	Innumerable	0	6.8	0	4	Onset not certain, acute symptoms for two weeks; sodium acid phosphate 1.34 gm. four times a day; later report, urine still sterile
					4/15/22	60	0.65	6.0	0	2	
					4/18/22	0	0.65	5.6	0	1	
					4/21/22	0	0.65	5.8	0	1	
4. V. C.	♀	9	4 yr.	Bacillus coli.....	9/ 7/22	Innumerable	0	6.2	0	1	Spina bifida occulta
						Innumerable	1.0	6.6	0		
						0	1.0	7.4	0	0	
					9/11/22	0	0	7.4	0	0	
5. I. M.	♀	14	3 yr.	Bacillus coli.....	10/14/22	Innumerable	0	6.8	0	3	
					10/15/22	..	1.0				
					10/17/22	0	1.0	6.8	0	1	
					10/25/22	0	0	6.8	0	1	
6. J. J.	♂	9	9 mo.	Staphylococcus aureus	11/ 3/22	Innumerable	1.5	6.8	0	4	Milky urine; hematuria developed one day after discontinuation of urotropin
					11/ 4/22	1,100	1.5	6.8	0	4	
					11/ 6/22	0	0	6.8	0	4	
					11/10/22	0	0	6.8	0	3	
					11/15/22	0	0	7.0	0	1	
7.	♀	3	2.5 yr.	Bacillus coli.....	1/20/23	Innumerable	0.75	7.2	0	3	
					1/26/23	15	0.75	6.6	1:100,000	1	
					1/31/23	0	0.75	7.0	1:100,000	1	
					2/ 7/23	0	0	7.0	0	0	
					2/26/23	0	0	7.0	0	0	
8. H. K.	♂	12	1 mo.	Bacillus coli.....	2/20/23	Innumerable	1.0	6.0	1:100,000	2	Secondary to Hirschsprung's disease
					2/26/23	30	1.0	5.4	0	1	
					3/ 1/23	0	1.0	6.0	0	1	
					3/ 5/23	0	0	0	0	0	
9. R. P.	♀	12	1 wk.	Bacillus coli.....	3/26/24	Innumerable	1.3	...	...	3	
					3/27/24	Innumerable	1.3	...	...	2	
					3/31/24	0	1.3	...	...	1	
					4/ 1/24	0	1.3	...	...	0	
10. M. H.	♀	11	3 yr.	Bacillus coli, Staphylococcus aureus	3/24/24	Innumerable	1.0	...	...	2	Roentgenogram of kidney and bladder, negative; no fever; specimen of urine resembled twenty-four hour bacterial culture
					3/28/24	0	1.0	...	...	1	
					3/29/24	0	0	...	...	1	
					3/31/24	0	0	...	...	1	

* In this column, ♀ indicates female; ♂, male.

of the local physician, but did not feel that dosage of urotropin up to 6 gm. should be given except with the control of the urine at least every other day.

Doses of from 4 to 6 gm. in twenty-four hours can be given only when large amounts of fluid are being taken. This was evident in Case 6, in which, as a result of the urotropin, the boy evidently had irritation of the stomach which prevented his taking fluids, and he developed very marked hematuria with considerable pain in the left side. The hematuria developed twenty-four hours after the urotropin was stopped, but probably there was still enough in the body to cause the disturbance. At no time was there formaldehyd in the urine, so that the hematuria must have been due to urotropin.

Another feature to be emphasized particularly is that formaldehyd was never present in concentration greater than 1:20,000, and it was usually less than 1:100,000. The attempt was always made to keep the urine between a hydrogen-ion concentration of 5.8 and 7, and to combine as much fluid with the urotropin as could be taken by the patient. Six patients with colon bacillus infection and four with staphylococcus infection were successfully treated. The one unsuccessfully treated had an infection caused by a *Bacillus mucosus capsulatus,* complicated by spina bifida, incontinence and residual urine. Even in this case the urine was made sterile with concentration of formaldehyd of only 1:50,000. The patient developed an acute infection, and with a discontinuation of the urotropin the organisms became innumerable in 0.5 c.c. of urine. In the other cases, the number of organisms in each cubic centimeter of urine was very markedly reduced, but the condition was not definitely cleared up.

COMMENT

This series of cases is presented in order to direct attention to the benefits of urotropin in cases of chronic pyelitis, and to emphasize particularly the good results from treatment without the presence of formaldehyd in concentrations supposed necessary by many observers. The impression given in a recent editorial in the *Journal of the American Medical Association* that urotropin is of little value, even in cases of urinary infections, cannot be subscribed to; on the contrary, it has a very definite use in clearing up urinary infections in children. Therapeutic effects were obtained even when the concentration of formaldehyd seemed insufficient to account for the favorable action.

6. THE USE OF CALCIUM CHLORID IN ACIDIFYING URINE

A method of acidifying urine in the treatment of pyelitis has long been looked for. The methods employed up to this time have consisted essentially in the giving of acids, hydrochloric, benzoic or acid phos-

phates. In our experience these, particularly the latter, have proved very unsatisfactory in that very little change could be produced in the reaction of the urine by small or moderate doses, and with large doses diarrhea usually resulted.

When calcium chlorid is used as a diuretic in patients with nephritis, it is found that the reaction of the urine swings very decidedly toward acidity. This is brought about by the excretion of the calcium ion through the bowel and the chlorid ion through the kidney. The chlorid excretion in the urine results in a very marked reduction of the hydrogen-ion concentration which can be controlled at a level of 5 and below. With the hydrogen-ion concentration of the urine definitely fixed, it becomes very much simpler to give hexamethylenamin in amounts that will produce antisepsis.

We have found that giving from 1 to 3 gm. of calcium chlorid four times a day at six-hour intervals will keep the urine of patients suffering from pyelitis constantly at a hydrogen-ion concentration of 5 or below; in so doing, the hexamethylenamin may be made the only variable which heretofore has not been the case. Ammonium chlorid can be used in similar dosage in place of calcium chlorid.

The rapid change of reaction of the urine is used by many in the treatment of pyelitis. Calcium chlorid is of great value in bringing about a rapid change from alkaline to acid urine.

In a recent study on the inhibition of growth of colon bacilli and staphylococci by rapid change of reaction, we found that the staphylococcus frequently was completely inhibited in its growth at a hydrogen-ion concentration of 5.2 in buffered broth. It seems probable, therefore, that if we can maintain a hydrogen-ion concentration of 4.5 to 5 constantly for a prolonged period of time, it may be possible to clear up infections with staphylococci by the control of reaction alone.

This change of reaction of the urine from a hydrogen-ion concentration of 7 plus to one of 5 to 4.5 is illustrated by the following case:

H. L., was admitted to the Clinic, June 24, 1924. The urine showed a hydrogen-ion concentration of 7.2. The next day the concentration was 7. Calcium chlorid, 4 gm. three times a day, was started. June 26, morning, noon and night specimens of urine showed the following hydrogen-ion concentrations, 6.6, 6.0, and 5.8. The hydrogen-ion concentration on June 27 was 5.4, and on June 28, it was 4.5.

CONCLUSIONS

1. In pyelitis of rabbits, alkalis definitely increase the output of urine and may have some direct effect on clearing up the infection.

2. There is no constant or essential difference in the reaction following injection of filtrates from organisms grown in acid or alkaline mediums.

3. A definite inhibition of growth was observed only when organisms growing in alkaline broth were transferred to acid broth.

4. In three cases studied, no beneficial effect was seen from the administration of acriflavin up to tolerance.

5. A series of cases of pyelitis treated with urotropin showed definite improvement without the concentration of formaldehyd ever reaching the point deemed essential by some other observers.

6. Calcium chlorid and ammonium chlorid are of great value in rapidly producing an acid urine.

LEUKOCYTOSIS IN VACCINATION *

KATSUJI KATO, M.D.

LOS ANGELES

During the epidemic of smallpox in Southern California in the early part of 1924, the Child Welfare Division of the Los Angeles City Health Department voluntarily vaccinated a large number of infants and children coming to its conferences. This afforded me an opportunity to study the changes in the cellular elements of blood following vaccination. From the very nature of these conferences, it has not been practicable to follow up the blood picture in single cases, as the majority of mothers were of the Mexican race and would not consent to repeated blood examinations. However, examinations were made at certain critical intervals and the results, therefore, are believed to be fairly representative of the general nature of leukocytosis due to vaccination.

REVIEW OF THE LITERATURE

The leukocyte changes following vaccination have been studied but scantily. It has been assumed by many that the blood picture in vaccination stimulates that which is seen in true variola. Brouardel,[1] one of the earliest observers, noted that the leukocytes were increased during the febrile remission between the periods of eruption and suppuration, but diminished during suppuration, and increase at this time or during desiccation signifying to him secondary infection. Verstraten [2] examined blood in eleven cases of variola and found that the leukocyte count reached its maximum during the stage of suppuration and during desiccation. Halla [3] observed that the leukocyte count was as high as 16,500 in one of his eleven patients on the fourth day of the disease, and concluded that there was a decided leukocytosis in the stage of suppuration. Pee [4] noted a leukocytosis of 20,000 during the early part of the eruption. Pick,[5] studying forty-two cases of variola, concluded that

* Received for publication, Sept. 29, 1924.

* From the Division of Child Welfare, J. D. Dunshee, M.D., Director, Department of Health, L. M. Powers, M.D., Commissioner.

1. Brouardel: Des variations de la quantité des globules blanc dans le sang des varioleux, etc., Gaz. méd. de Paris, **11**:141, 1874.

2. Verstraten: Note sur le sang des malades atteints de variola, Bull. de l'Acad. roy. de Belgique 1875, p. 1005.

3. Halla: Ueber die Haemoglobingehalt des Blutes und die qualitativen Verhaltnisse der rothen und weissen Blutkorperchen bei acuten fiberhaften Krankheiten, Ztschr. f. Heilk. **4**:198, 1883.

4. Pee: Untersuch. ueber Leukocytosis, Inaug.-Diss., Berlin, 1890.

5. Pick, R.: Untersuch. über des quantitativen Verhalten der Blutkorperchen bei Variola und ihren Complicationen, Arch. f. Dermat. u. Syph. **25**:63, 1893.

infection with smallpox in itself causes no leukocytosis but that it may be caused by secondary pyogenic infection during the stage of suppuration. Von Linbeck [6] on the basis of his findings in two cases disagrees with Pick. Hayem [7] found leukocytosis beginning the second or third day of eruption and gradually increasing during suppuration up from 28,000 to 30,000. Courmont and Montagard [8] examined twenty-nine patients with variola, all of which were accompanied by a leukocytosis due to mononucleosis which he believed to be of diagnostic importance. Weil [9] says that the acme of the leukocytosis is at the time of the appearance of the eruption or at vesiculation, but that the typical leukocytosis is modified more or less by intercurrent infections. Furguson [10] found leukocytosis occurring on the ninth day of the disease, but decreasing from that time on unless complications set in. He also noted that the qualitative changes consisted in the increase in mononuclear elements, with a relative though not absolute decrease in polymorphonuclear neutrophils. The leukocyte changes at various intervals have been formulated by Magrath, Brickerhoff and Bancroft [11] as follows: (1) Hyperleukocytosis during incubation; (2) hypoleukocytosis, relative or absolute, during onset and febrile remission; (3) hyperleukocytosis during formative evolution of eruption; (4) relative hypoleukocytosis at the height of pustulation; (5) hyperleukocytosis during desiccation. The findings thus briefly summarized show that there is no absolute agreement in the nature of leukocytosis in variola vera. It is sufficient to remark that in true smallpox there is a definite leukocytosis at certain stages of the disease, and that it is due to an increase in mononuclear rather than polymorphonuclear elements.

As to vaccinia and vaccination, the knowledge of leukocyte changes is again very scanty. Sobotka [12] examined the blood of forty-three children after vaccination, making the following observations: The red cells and hemoglobin showed no constant variation, and usually remained normal. Vaccination always caused leukocytosis, beginning usually on the third or fourth day after inoculation and gradually falling until the seventh or eighth day when the leukocytes were frequently subnormal. From the tenth or twelfth day a secondary leukocytosis regu-

6. Von Linbeck: Grundriss einer klin. Path. des Blutes, Jena, 1896.

7. Hayem: Du sang et de ses alterations anatomiques, Paris, 1899.

8. Courmont et Montagard: Les leucocytoses dans la variola, J. de physiol. et path. gén. **2**:557, 1900.

9. Weil, F.: La sang et les réactions défensives de l'hémopoise dans l'infection variolique, Thèse de Paris, 1901.

10. Furguson: The Leukocytosis of Variola, J. Path. & Bacteriol. **8**:411, 1903.

11. Magrath, G. B.; Brickerhoff, W. R., and Bancroft, I. R.: The Leukocyte Reaction in Variola, J. M. Res. **11**:247, 1904.

12. Sobotka: Zur Kentniss des Vaccine-processes, Ztschr. f. Heilk. **14**:349, 1893.

larly appeared, lasting from two to six days and showing close relation to the activity of the virus and the number of the pustules. The height of the first leukocytosis varied between 12,000 and 23,000; that of the second between 10,000 and 17,500, while in the intermediate period the cells fell as low as 3,500. In uncomplicated cases the lowest figures usually corresponded to the highest temperatures, the leukocytosis preceding the local and general manifestations of vaccinia by several days. Again, Fürst [13] points out that there is an increase in the number of leukocytes in the blood during the vaccination period. This increase, according to his findings, takes place about the third day when the local eruption is first developing, and again when the surrounding inflammation is at its height. The leukocytosis diminishes rapidly with the fall of temperature in the early part of the second week, and appears to be proportional to the severity of the symptoms.

PRESENT FINDINGS

The present investigation is based on the findings of blood examination in 153 infants under 18 months of age, all of whom were vaccinated during the Infant Welfare Conferences. The inoculation was accomplished by means of a scarifier which was rapidly twisted through a drop of the virus. Only one inoculation was made in each patient, the site of inoculation being usually over the point corresponding to the insertion of the deltoid muscle of the left upper arm. The total white blood count may be tabulated as follows:

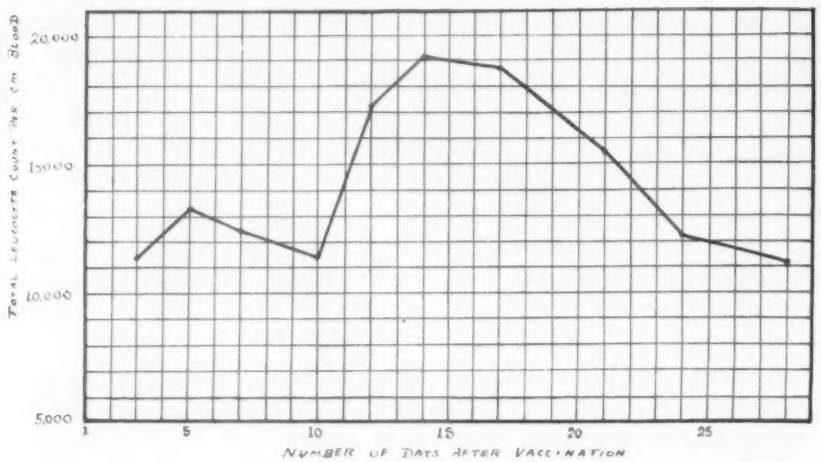
TABLE 1.—*White Blood Count of One Hundred and Fifty-Three Infants*

No. Days After Vaccination	No. Cases	Total White Count
3	22	11,410
5	18	13,300
7	17	12,400
10	10	11,440
12	19	17,250
14	20	19,140
17	15	18,800
21	20	15,410
24	8	12,320
28	4	11,100

Table 1 is graphically reproduced in the chart. It is apparent from these figures that there is a slight initial leukocytosis on the fifth day after inoculation, reaching 13,300 per cubic millimeters of blood. On the tenth day after vaccination, however, the count falls almost to the normal level, but on the twelfth day, it rises again and initiates the secondary or true leukocytosis of vaccination. The average count in our cases at the height of this secondary leukocytosis was 19,140, the

13. Fürst: Die Pathologie der Schutzpocken-Impfung, Berlin, 1896, p. 21.

highest being 27,400 and the lowest 14,400, which occurred on the fourteenth day. From this time on the count gradually falls and by the end of the fourth week after vaccination, the count reaches the normal level. The fact that leukocytosis corresponds with the nature



White blood count of 153 infants.

of reaction and severity of lesions seems to be well understood. The initial or primary leukocytosis is merely an indication of general reaction, while the secondary leukocytosis which begins on the twelfth day is the true leukocytosis of vaccination. Clinically it is well known that the average vaccination lesion reaches its maturity about the time when the secondary leukocytosis reaches its height. When the leukocyte count falls to the normal level, the crust from the lesion falls off, leaving a slightly pinkish scar.

As to the differential count of the white cells, the data are tabulated in Table 2.

TABLE 2.—*Differential White Cell Count*

Days after vaccination	3	5	7	10	12	14	17	21	24	28
Cells:										
Small lymphocytes	46	50	48	49	56	47	50	48	52	54
Large lymphocytes	12	11	10	9	12	16	12	11	13	12
Polymorphonuclear neutrophils	27	25	26	27	21	24	24	25	23	23
Polymorphonuclear eosinophils	3	2	2	1	1	2	2	3	1	1
Transitional cells	7	8	8	8	6	6	6	7	6	6
Large mononuclears	5	4	6	6	4	4	6	6	5	4
Myelocytes neutrophils	0	0	0	0	0	1	0	0	0	0

The uniformity of the differential counts at various intervals after vaccination is a striking feature in Table 2. It has been assumed almost universally that the leukocytosis of vaccination is due to the relative

increase in the percentage of the polymorphonuclear cells, as it seems to depend on the pustulation of the lesions. From our data, however, it becomes evident that in the vaccination leukocytosis there is no polymorphonucleosis. The polymorphonuclear neutrophils show the percentage figures from 21 to 27, a perfectly normal picture. The eosinophils give a rather constant percentage with the figures ranging from 1 to 3 per cent. The small lymphocytes give the figures from 46 to 58 per cent., which is about the normal count during infancy. The large lymphocytes vary between 9 and 16 per cent., which is also normal. In brief, it may be said that there is no abnormal variation in the differential count of the white cells after vaccination.

SUMMARY AND CONCLUSIONS

1. A study of the nature of leukocytosis following vaccination is made, following examination of the blood of 153 infants under 18 months of age.

2. Our data show that vaccination is always accompanied by a definite leukocytosis, both primary and secondary.

3. The primary leukocytosis begins on the third day after inoculation, and shows the result of general reaction of the organism toward the invading virus. The total white count in the primary leukocytosis is not as high as in the secondary leukocytosis. The duration of the primary leukocytosis is about four days, reaching its maximum on the fifth day after inoculation.

4. The secondary leukocytosis is the true leukocytosis of vaccination, which begins on the twelfth day, lasting from seven to ten days. The total white count was at its maximum on the fourteenth day after inoculation and was much higher than that found in the primary leukocytosis.

5. The differential count made at various intervals after inoculation shows no significant variation from the normal.

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THE SIGNIFICANCE OF CRANIOTABES AND BOWING OF THE LEGS*

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In his recent monograph on rickets, Hess [1] states that: "Craniotabes is valuable in establishing the diagnosis of rickets, but, unless the course of the softening has been followed for several months it is often difficult to differentiate it from the craniotabes encountered in very young infants. Whether bowed legs are always due to rickets is by no means certain; it is a deformity that may appear after all other signs have disappeared, or, at times, in overweight children who have manifested no other signs of rickets."

REVIEW OF THE LITERATURE

Since craniotabes develops in many infants suffering from rickets, it is frequently taken for granted that it is pathognomonic of the disease. Kassowitz [2] was strongly of this opinion, and believed he could cure it by the administration of phosphorus. There is, however, a softening of the cranial bones in young and premature infants, first described by Elsasser [3] in 1843, which greatly resembles craniotabes, and which is not generally accepted as due to rickets. In reporting the incidence of rickets in very young infants, a great deal of significance is attached to the presence of craniotabes, and it is therefore of importance to determine the relation of rickets to its pathogenesis. It is hardly necessary to go into a lengthy account of the pros and cons of this subject. A few citations will suffice to indicate the trend of opinion. Friedleben [4] showed that craniotabes was often present during the first weeks of life, and Bohn [5] thought that these areas of softening were not rachitic, but that those which appeared after the second or third month were. Huenekens,[6] in a report of a series of cases of rickets

* Received for publication, Oct. 3, 1924.

* From the Home for Hebrew Infants.

1. Hess, A. F.: Abt's Pediatrics, Philadelphia, W. B. Saunders Company, Vol. 2, 1924.
2. Kassowitz, M.: Wien. med. Jahrb. 1884.
3. Elsasser, C. L.: Der Weiche Hinterkopf, 1843.
4. Friedleben, A.: Jahrb. f. Kinderh. **3**:1860.
5. Bohn: Jahrb. f. Kinderh. **22**:1884.
6. Huenekens, E. J.: Journal-Lancet **37**:804 (Dec. 15) 1917.

occurring before the age of 4 months in premature and twin infants, mentions craniotabes as the earliest sign, and in three instances noted its presence at the age of 6 weeks. DeBuys,[7] in a study of a group of breast-fed infants, unquestionably regards it as a positive sign of rickets. Dalyell and Mackay,[8] members of the British commission who investigated rickets in Vienna, state that: "In practice craniotabes can be accepted as evidence of rickets," and although granting that congenital softening of the cranial bones exists, believe that the two conditions can be differentiated by differences in type and distribution. In their study they have diagnosed all patients over the age of 3 months with craniotabes as rachitic.

Pommer,[9] as well as Wieland,[10] showed definitely by microscopic examinatoin that the softening of the cranial bones in the new-born were not rachitic but osteoporotic. Schmorl,[11] the great authority on the pathology of rickets, in over one hundred new-born and premature infants coming to necropsy, found no histologic evidence of rickets in the bones. In puppies, osteoporosis was induced many years ago by a simple lack of calcium in the diet, furthermore, when rats are deprived of the fat-soluble vitamin [12] they develop osteoporosis and not rickets, which finding was determined by microscopic examination. Dalyell and Mackay [8] at necropsy in seven infants with craniotabes found that rickets was present in all, but they omit to state the ages of the infants; if they were under 4 months their findings would have great significance.

DATA OF RECORDS

In view of the fact that we have complete records in regard to rickets of a large group of infants with craniotabes, and that the examinations and tests have extended over exceptionally long periods, it seemed worth while to present the data, and to attempt to draw conclusions of their significance. The infants included in our study have been examined every month by the same person, so that the clinical findings are not open to error through subjective interpretation. It is important that the examination for craniotabes be carefully carried out, as the area is often small and sharply circumscribed, and may easily

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7. DeBuys, L. R.: A Clinical Study of Rickets in the Breast-Fed Infants, Am. J. Dis. Child. **27**:149 (Feb.) 1924.

8. Dalyell, E. J., and Mackay, M. M.: Notes on the Clinical Signs of Infantile Rickets as Observed in Vienna, Special report No. 77 Medical Research Council, 1923.

9. Pommer, G.: Untersuchungen ueber Osteomalacie und Rachitis, Leipzig, 1885.

10. Wieland, E.: Ergebn. d. inn. Med. u. Kinderh. **6**:64, 1910.

11. Schmorl, G.: Ergebn. d. inn. Med. u. Kinderh. **4**:403, 1909.

12. Hess, A. F.; McCann, G. F., and Pappenheimer, A. M.: J. Biol. Chem. **47**:395 (July) 1921.

be overlooked. In this respect this condition differs from beading of the ribs, which occurs always at the same site, so that if it is not found one can be certain of its absence. Craniotabes, however, may be located in any part of the parietal bones, and occasionally in the upper part of the occipital and temporal bones, so that one must be cautious before declaring it absent. The softening to which we have reference is not that which occurs along the sagittal suture, the origin of which is osteoporotic rather than rachitic, but that found in the occipital region. Moreover, the degree of the softening varies as well as the area; the very slightest degree we have omitted and classified as negative.

The reason we are reporting this study is because it has been carried out with the aid of roentgenologic examination of the epiphyses, and chemical examination of the blood for inorganic phosphorus. So far as we are aware there has been no previous report in which a chemical examination has been made, nor any fortified by routine and consecutive roentgenograms. In view of the fact that the nature of craniotabes is open to question, it seemed of particular value to control its occurrence by these two new and valuable diagnostic criteria. This is especially true of the examination for inorganic phosphorus, as this is a sign which appears early and is therefore well suited to shed light on the nature of these cases of cranial softening which are found in the first three or four months of life.

Two hundred and eighty-nine infants were studied; their ages at the time of the first examination varying from a few days to 1 year, 126 being under 4 months of age. One hundred and twenty-nine infants at some time had craniotabes, of whom twenty-five had what we considered too few examinations to be included in this group, so that we have tabulated the observations on ninety-six cases of craniotabes. We endeavored to divide these cases into several age groups, and to correlate the craniotabes with the clinical and laboratory observations of rickets. At first we arbitrarily formed three groups, namely, those 3 months of age and under, those 6 months of age and over, and an intermediate group of from 3 to 6 months of age. It was then found more logical to form only two groups, those under 4 months of age, and those over this age. Sixty-eight children, or about two-thirds, fell into the first group and twenty-eight or about one-third, into the second. Of the former (Table 1), practically none showed coincident rickets, as indicated by clinical (beading of the ribs), roentgenographic or chemical evidences. No patient had more than a very slight degree of beading, which must be disregarded as indicative of rickets in such young infants.[1] One patient showed slight rickets by roentgenogram, and only one had as low a percentage of inorganic blood phosphorus as 3.7 mg., which we regard as just at the rachitic level. There were

TABLE 1.—*Relation of Craniotabes to Other Signs of Rickets in Infants Under Four Months*

	Craniotabes, First Examination			Coincident Signs of Rickets			
Case	Date	Age, Weeks	Degree	Beading	Roentgenogram	Phosphorus (Inorganic)	Comment
1	Sept. 16	2	Slight	Negative	Negative	...	
2	Mar. 15	4	Slight	Negative	Negative	3.8	
3	April 23	8	Slight	Negative	Negative	4.3	
4	Feb. 28	6	Slight	Slight	Negative	3.9	
5	Mar. 12	8	Slight	Slight	Negative	3.7*	
6	April 30	4	Slight	Slight	Negative	4.1	
7	Mar. 3	6	Slight	Negative	Negative	4.0	
8	Oct. 22	5	Slight	Negative	Negative	...	
9	May 14	8	Moderate	Negative	Negative	4.5	
10	May 30	2	Marked	Negative	Negative	...	
11	Oct. 21	8	Slight	Negative	Negative	...	Twin
12	Jan. 15	4	Slight	Negative	Negative	4.5	
13	April 1	6	Slight	Negative	Negative	...	
14	May 18	6	Marked	Negative	Negative	...	
15	June 29	7	Slight	Negative	Negative	...	Premature
16	Sept. 2	8	Marked	Negative	Negative	...	Premature
17	Jan. 30	2	Slight	Negative	Negative	...	
18	Feb. 25	5	Marked	Negative	Negative	...	
19	Aug. 16	8	Marked	Negative	Negative	4.3	
20	Nov. 30	4	Slight	Negative	Negative	...	
21	Dec. 2	4	Slight	Negative	Negative	4.0	
22	July 27	4	Marked	Negative	Negative	...	
23	Aug. 7	4	Slight	Negative	Negative	...	
24	Dec. 19	2	Slight	Negative	Negative	...	Twin
25	Sept. 12	6	Moderate	Negative	Negative	...	
26	Oct. 20	4	Marked	Negative	Negative	...	
27	Dec. 15	2	Marked	Negative	Negative	...	Twin
28	Dec. 15	2	Marked	Negative	Negative	...	Twin
29	May 16	10	Slight	Negative	Negative	4.1	
30	Oct. 3	4	Marked	Negative	Negative	...	
31	Nov. 17	2	Marked	Negative	Negative	...	Twin
32	Nov. 17	2	Marked	Negative	Negative	...	Twin
33	Aug. 1	8	Moderate	Negative	Negative	5.4	Premature
34	Nov. 17	8	Slight	Negative	Negative	...	Premature
35	Sept. 30	4	Slight	Negative	Negative	...	
36	June 15	2	Slight	Negative	Negative	4.5	
37	Feb. 16	8	Slight	Slight	Negative	...	
38	Mar. 2	4	Slight	Negative	Negative	...	Twin
39	Mar. 2	4	Slight	Negative	Negative	...	Twin
40	Mar. 2	4	Slight	Negative	Negative	...	
41	May 6	10	Slight	Negative	Negative	4.7	
42	May 6	6	Moderate	Negative	Negative	4.5	
43	Mar. 23	4	Slight	Negative	Negative	4.4	
44	April 29	4	Slight	Negative	Negative	4.6	
45	Jan. 21	4	Marked	Negative	Negative	...	
46	Nov. 17	6	Slight	Slight	Negative	...	
47	Mar. 14	8	Slight	Negative	Negative	...	
48	June 13	3	Slight	Negative	Negative	5.1	
49	May 15	8	Slight	Negative	Negative	4.0	
50	Dec. 11	6	Slight	Slight	Negative	...	
51	April 25	12	Slight	Slight	Negative	3.9	
52	June 13	8	Slight	Negative	Negative	5.1	
53	Mar. 13	13	Slight	Negative	Negative	...	
54	Aug. 3	2	Marked	Negative	Negative	...	
55	Sept. 11	4	Slight	Negative	Negative	...	
56	Sept. 12	8	Slight	Negative	Negative	...	
57	Mar. 5	2	Marked	Negative	Negative	...	
58	June 20	6	Marked	Negative	Negative	...	
59	June 25	14	Slight	Negative	Negative	...	
60	May 9	13	Moderate	Negative	Negative	4.1	
61	April 7	12	Slight	Slight	Negative	4.3	
62	April 12	12	Moderate	Negative	Negative	4.1	
63	Oct. 1	14	Marked	Slight	.....	...	Twin, premature
64	Oct. 1	14	Slight	Slight	.....	...	Twin, premature
65	Jan. 30	14	Slight	Slight	Slight†	...	
66	Aug. 31	14	Marked	Negative	Negative	...	Premature
67	Feb. 27	12	Marked	Negative	Negative	...	
68	Mar. 23	14	Slight	Negative	Negative	4.7	

* Youngest case to show low inorganic phosphorus.
† Youngest case to show rickets by roentgenogram.

twenty-eight infants, aged over 4 months, with craniotabes. (Table 2), and only seven of these did not have coincident rickets as judged by the same criteria. All developed rickets soon thereafter, and in twenty-seven the cranial softening lasted as long as the rickets.

Thus it will be seen that under 4 months of age the softening of the cranial bones is usually not associated with rickets, whereas over this age in at least 75 per cent. of the cases there is this association.

One of the main reasons for the confusion existing on the subject of craniotabes and rickets is that there has been no agreement on the fundamental question of what does, and what does not, constitute

TABLE 2.—*Relation of Craniotabes to Other Signs of Rickets in Infants Over Four Months*

	Craniotabes, First Examination			Coincident Signs of Rickets			
Case	Date	Age, Months	Degree	Beading	Roentgenogram	Phosphorus (Inorganic)	Comment
1	May 16	4	Moderate	Moderate	Negative	...	
2	Nov. 19	5	Slight	Negative	Negative	...	
3	Dec. 31	4	Marked	Slight	Slight	...	
4	Feb. 2	4	Marked	Slight	Healing	...	Twin
5	Feb. 2	4	Marked	Moderate	Healing	4.4	Twin
6	Mar. 21	4	Marked	Slight	Slight	3.4	
7	Jan. 2	5	Marked	Slight	Negative	4.0	
8	Feb. 5	5	Marked	Slight	Negative	...	
9	Jan. 2	5	Slight	Slight	Negative	3.1	
10	Sept. 6	7	Slight	Negative	Negative	...	
11	May 28	7	Marked	Slight	Moderate	...	Premature
12	Jan. 8	8	Marked	Slight	Negative	4.0	
13	Dec. 28	5	Marked	Negative	Negative	...	
14	May 9	6	Marked	Slight	Moderate	...	
15	Dec. 30	7	Moderate	Slight	Moderate	...	
16	June 15	5	Marked	Moderate	Negative	4.1	
17	Oct. 22	5	Slight	Negative	Negative	...	
18	Feb. 23	8	Moderate	Marked	Moderate	...	
19	Feb. 2	6	Slight	Slight	Moderate	...	
20	May 4	7	Slight	Slight	Slight	2.9	
21	April 22	6	Slight	Moderate	Negative	2.5	
22	Feb. 6	7	Slight	Marked	Slight	...	
23	May 23	7	Marked	Moderate	Slight	3.7	
24	April 20	10	Slight	Marked	Moderate	2.5	
25	Feb. 26	11	Moderate	Slight	Moderate	...	
26	Feb. 20	12	Slight	Slight	Moderate	2.4	

rickets. For instance, although all are agreed that in rickets there is a lowering in percentage of the inorganic blood phosphorus, as shown by Iversen and Lenstrup,[13] as well as by Howland and Kramer,[14] all are not in accord as to what degree this percentage must reach to indicate rickets. Some claim the level to be 3.75 mg. per hundred cubic centimeters, while recently Anderson[15] stated that in normal infants it may reach this level. Another ground for confusion is the fact that, although it is well known that craniotabes may disappear before the appearance

13. Iversen, P., and Lenstrup, E.: Forhandl. av. Forste Nordiske, Kongres for Pædiatri, 1920.

14. Howland, John, and Kramer, Benjamin: Calcium and Phosphorus in the Serum in Relation to Rickets, AM. J. DIS. CHILD. **22**:105 (July) 1921.

15. Anderson, G. H.: Calcium and Phosphorus Content of Blood in Normal and Rachitic Children, Brit. J. Child. Dis. **21**:107 (Jan.-March) 1924.

of rickets as indicated by accepted standards, yet all do not agree that this proves that the softening is nonrachitic. It is argued that rickets attacks those bones which are growing most rapidly, and as this applies to the cranial bones during the first few months of life, they are accordingly attacked by the disorder. As the child grows older, the rate of cranial growth is diminished, so that the craniotabes tends to heal. This argument would hold were it a fact that craniotabes always behaved in this manner, yet all observers have noted craniotabes in rachitic infants aged over 4 months, which persists until the rickets is healed, which may not occur until the age of 12 months. Moreover, there are infants under 4 months of age with craniotabes who have no other signs of rickets, in whom the softening disappears only to reappear later when rickets does develop.

THERAPEUTIC TEST

A much emphasized point in regarding all craniotabes as rachitic is the fact that it disappears readily under antirachitic treatment. Meyer [16] was of this opinion because he healed the softening with ultraviolet light. Dalyell and Mackay [8] cured it by means of cod liver oil. These authors also noted that in a great many instances it disappeared spontaneously during the summer months. These are absolutely in accord with our observations. We must not lose sight of the fact, however, that these several agencies cure conditions which are other than rachitic. Hume,[17] and also Goldblatt and Soames,[18] showed that ultraviolet light can prolong normal growth in rats that are on a diet deficient in the fat-soluble vitamin, which has been shown to produce osteoporotic rather than rachitic changes in the bones.

OBSERVATIONS

In this connection we present the observations on nine infants with craniotabes (Table 3), who from the time of the first examination until the disappearance of the softening received no antirachitic treatment, and in whom, notwithstanding, the condition disappeared during the winter months, namely, November to April inclusive. At no time during this period did the infants show any sign of rickets. These observations were made at approximately monthly periods and none were omitted. The phosphorus content in every case where the estimation was performed was well above the rachitic level, and the roentgenograms were negative. To our minds this definitely establishes the existence of a nonrachitic craniotabes.

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16. Meyer, L. F.: Internat. Clinics **4**:176, 1921.
17. Hume, E. M.: Lancet **2**:1318 (Dec. 23) 1922.
18. Goldblatt, H., and Soames, K. M.: Lancet **2**:1321 (Dec. 23) 1922.

It is not suggested that the softening of the cranial bones in infants under 4 months of age is due to a lack of the fat-soluble vitamin; we believe that the actual cause of this condition has yet to be determined. We do feel, however, that early craniotabes usually is not rachitic, basing our opinion on the fact of the lack of the established signs of coincident rickets. It seems especially significant that the content of inorganic phosphorus in the blood was not diminished, for its diminution is one of the earliest evidences of rickets. The microscopic findings of Pommer, of Wieland and also of Schmorl are in agreement with this point of view. Nonrachitic softening may persist until the child is aged 7

TABLE 3.—*Cases of Craniotabes Disappearing Spontaneously During Winter, (November to April) No Other Signs of Rickets Having Developed*

Case	Date	Age, Weeks	Degree	Beading	Roentgenogram	Phosphorus (Inorganic)
1	Sept. 16	2	Slight	Negative	Negative	...
	Oct. 21	6	Slight	Negative	Negative	...
	Nov. 23	10	Negative	Negative	Negative	4.1
2	Jan. 30	2	Slight	Negative	Negative	...
	Mar. 6	8	Slight	Negative	Negative	...
	April 10	12	Slight	Slight	Negative	...
	May 15	16	Negative	Slight	Negative	...
3	Aug. 16	8	Marked	Negative	Negative	...
	Sept. 23	12	Marked	Slight	Negative	...
	Oct. 28	16	Slight	Slight	Negative	...
	Dec. 4	21	Negative	Slight	Negative	4.3
4	Dec. 2	5	Slight	Negative	Negative	...
	Jan. 2	9	Slight	Negative	Negative	4.0
	Feb. 7	14	Negative	Negative	Negative	3.8
5	July 27	3	Marked	Negative	Negative	...
	Aug. 31	7	Marked	Negative	Negative	...
	Oct. 4	12	Slight	Negative	Negative	...
	Nov. 18	17	Negative	Slight	Negative	4.3
6	Sept. 13	7	Slight	Negative	Negative	...
	Dec. 18	19	Negative	Slight	Negative	4.5
7	Aug. 31	2	Marked	Negative	Negative	...
	Oct. 4	7	Slight	Negative	Negative	...
	Nov. 6	11	Negative	Negative	Negative	4.0
8	Oct. 3	4	Marked	Negative	Negative	...
	Dec. 3	12	Marked	Slight	Negative	...
	Jan. 14	18	Negative	Negative	Negative	...
9	Mar. 23	14	Slight	Negative	Negative	...
	May 8	20	Negative	Slight	Negative	4.7

months, without his developing rickets. Since nearly all artificially fed infants develop this disorder if not protected, rickets may follow and even be accompanied by the development of craniotabes and yet have no etiologic connection with the softening of the skull which was noted during the first 4 months of life. There are, undoubtedly, many such cases, and it is manifestly impossible to differentiate the two conditions at this late period, unless the course of the softening has been observed over a period of several months.

BOWING OF THE LEGS

Bowing of the legs seems to be almost universally ascribed to rickets; to such an extent is this so that it is difficult to find any references to

the contrary. It seems also agreed that, whereas craniotabes is an early sign of rickets which occurs in young infants, bowing occurs in older children and is a late sign of the disease. In fact, many observers consider it a residuum of rickets rather than a sign of active disease. In view of this prevailing opinion, our observations may gain added interest.

The bowing to which we have reference is that which is especially marked in the lower third of the tibia, and no case is included in which the deformity did not markedly exceed the normal curvature.

The technic of examination is of importance, as, depending on it bowing may be either overlooked or exaggerated. The child should be

TABLE 4.—*Bowing of Legs Without Other Signs of Rickets*

	Previous Course in Regard to Rickets *				First Appearance of Bowing		Coincident Signs of Rickets			Subsequent Course in Regard to Rickets †						
Case	Age, Months	Beading	Roentgenogram	Phosphorus (Inorganic)	Age, Months	Weight, Lbs.	Beading	Roentgenogram	Phosphorus (Inorganic)	Age, Months	Beading	Roentgenogram	Phosphorus (Inorganic)	Stood Age, Months	Number of Examinations	Duration, Months
1	11	Slight	Neg.	4.1	12	20	Neg.	Neg.	4.0	13	Neg.	Neg.	...	9	5	5
2	10	Neg.	Neg.	3.8	12	19	Neg.	Neg.	...	14	Neg.	Neg.	...	—	8	12
3	6	Neg.	Neg.	4.5	8	14	Neg.	Neg.	...	12	Neg.	Neg.	...	—	6	12
4	7	Neg.	Neg.	...	9	16	Neg.	Neg.	...	14	Neg.	Neg.	4.0	—	10	13
5	9	Neg.	Neg.	...	10	18	Neg.	Neg.	...	13	Neg.	Neg.	...	9	4	4
6	14	Neg.	Neg.	...	15	21	Neg.	Neg.	...	18	Neg.	Neg.	...	14	8	8
7	6	Slight	Neg.	4.1	10	19	Slight	Neg.	...	12	Neg.	Neg.	...	—	4	12
8	10	Slight	Neg.	4.0	14	21	Neg.	Neg.	...	20	Neg.	Neg.	...	10	4	13
9	2	Slight	Neg.	...	3	9	Slight	Neg.	4.5	14	Slight	Neg.	...	14	5	12
10	2	Neg.	Neg.	4.7	7	17	Slight	Neg.	...	12	Slight	Neg.	...	12	3	10
11	6	Neg.	Neg.	4.6	10	18	Neg.	Neg.	...	12	Neg.	Neg.	...	—	5	11
12	6	Neg.	Neg.	5.1	8	17	Slight	Neg.	...	14	Slight	Neg.	...	11	6	12
13	2	Neg.	Neg.	...	5	14	Slight	Neg.	4.5	8	Neg.	Neg.	...	—	4	6
14	11	Slight	Neg.	4.5	15	19	Slight	Neg.	...	—	—	—	...	11	4	13

* Refers to last examination showing signs of rickets. If rickets was absent the examination just previous to the appearance of bowing was included.

† Refers to first appearance of rickets. If rickets was absent, the last examinations were included.

placed on its back with legs extended, feet vertical and parallel. The examiner must be careful not to hold the legs just above the ankles, otherwise he may obscure the curvature. Furthermore, if the feet are held inverted and not parallel, the bowing will appear exaggerated; on the contrary if they are everted it will be diminished.

Among two hundred and eighty-nine infants fifty-four developed bowlegs. In Table 4 the data are presented of fourteen infants with marked bowing, who have been followed for periods of from four to twelve months. Not one of these infants had rickets as judged by clinical and laboratory criteria, nor did they suffer from this disorder before the deformity developed. Any case in which there was the slightest evidence of rickets during the entire period of observation has

been excluded from this group. For this reason we believe that this series, an unusual one, establishes the existence of a nonrachitic bowing of the legs.

In this connection attention may be directed to certain cases in Table 5 (Cases 2, 14 and 15) which tabulates the data of forty children with bowlegs who at some time or other did have rickets. It will be noted that in these instances the deformity appeared from four to eight months before the onset of rickets. In view of this interval, it is hardly probable that this bowing was a rachitic process, especially when we consider that this deformity is one of the late signs of the disease.

The majority of the children developed curvature of the legs toward the end of the first year or even later. There were, however, sixteen who showed marked bowing at 6 months or earlier. In thirty-three, that is, about 60 per cent., it appeared before 12 months, and in twenty-one after this age.

It is generally believed that the main cause of bowing is rickets associated with heavy weight and early standing. The weights throughout this series show that very few of the children were overweight, and that only thirteen stood before bowing developed.

Although craniotabes usually responds to antirachitic treatment (in one infant the softening disappeared after twelve days' treatment with the mercury vapor lamp), bowing does not yield readily to such treatment. Most of the cases are rectified spontaneously later, in spite of the fact that the children are walking. It is difficult to suggest what are the factors which influence the disappearance or the persistence of the deformity. Decrease in the rate of growth is certainly of importance. Furthermore, there does not seem to be any distinction in clinical course between the rachitic and the nonrachitic forms of this deformity; in our experience either condition may persist or spontaneously disappear.

Some investigators are of the opinion that craniotabes is caused by syphilis.[19] All the children in this institution are tested by the Wassermann reaction, and, strange to state, almost all react negatively,[20] so that in these cases syphilis may be excluded as the etiologic factor in the production of either craniotabes or bowing.

SUMMARY

The significance of craniotabes in rickets is still undecided. Some believe that all craniotabes is due to rickets, others are of the opinion that the condition, when it occurs in very young infants, is not of rachitic origin. Previous studies have been based on a consideration of this sign in its relation to pathologic changes found in the bones, and to the

19. Marfan, P.: Maladies des Os, Paris, Bailliere et Fils, 1912.

20. Barenberg, L. H., and Rosenberg, P.: Incidence of Wassermann Reaction in a Large Child-Caring Institution, Arch Pediat. **39**:23 (Jan.) 1922.

TABLE 5.—*Bowing of Legs Associated with Other Signs of Rickets*

Case	Previous Course in Regard to Rickets *				First Appearance of Bowing		Coincident Signs of Rickets			Stood	No. of Examinations	Duration, Months	Comment
	Age, Mo.	Beading	Roentgenogram	Phosphorus (Inorganic)	Age, Mo.	Weight, Pounds	Beading	Roentgenogram	Phosphorus (Inorganic)	Age, Mo.			
1	5	Negative	Negative	...	6	12	Slight	Negative	4.0	—	13	23	
2	10	Negative	Negative	...	14	19	Negative	Negative	. .	12	7	11	Bowing appeared four months before rickets
3	7	Slight	Negative	...	9	16	Slight	Slight	...	—	9	14	
4	13	Negative	Slight	3.4	18	22	Slight	Negative	...	11	9	15	
5	7	Moderate	Negative	3.7	8	15	Moderate	Negative	...	—	7	10	
6	5	Slight	Negative	4.1	7	16	Slight	Negative	...	—	8	12	
7	20	Slight	Moderate	3.7	22	21	Negative	Negative	3.8	20	12	22	Twin
8	9	Negative	Negative	3.5	12	22	Negative	Negative	...	12	9	10	Bowing appeared after rickets was healed
9	14	Slight	Moderate	...	15	19	Slight	Moderate	...	—	10	8	Premature
10	7	Negative	Negative	...	8	17	Negative	Negative	...	—	—	—	
11	19	Marked	Moderate	...	20	17	Moderate	Marked	...	16	20	20	
12	—	—	—	...	9	18	Slight	Negative	...	12	8	7	
13	18	Slight	Moderate	2.8	19	23	Slight	Marked	3.2	17	14	18	
14	4	Negative	Negative	...	5	16	Negative	Negative	4.1	—	9	9	Bowing appeared five months before rickets
15	5	Slight	Negative	...	6	13	Slight	Negative	...	—	15	22	Bowing appeared eight months before rickets
16	—	—	—	...	6	15	Slight	Moderate	...	—	7	7	
17	13	Slight	Negative	...	14	18	Slight	Moderate	3.7	12	11	12	
18	13	Moderate	Moderate	3.7	14	21	Slight	Negative	4.1	—	12	13	
19	6	Slight	Negative	4.3	8	14	Slight	Negative	4.3	—	9	9	
20	4	Marked	Slight	...	5	9	Moderate	Slight	...	—	17	18	
21	13	Negative	Slight	...	14	20	Negative	Negative	...	11	21	23	
22	9	Slight	Slight	4.0	10	18	Slight	Slight	...	8	9	9	Bowing appeared after rickets was cured
23	5	Negative	Negative	3.5	14	22	Negative	Negative	...	15	11	24	
24	12	Slight	Negative	4.1	13	19	Slight	Negative	4.2	11	10	10	Bowing persisted in spite of healing of rickets
25	3	Negative	Negative	...	4	10	Negative	Slight	...	—	13	13	
26	3	Slight	Negative	...	4	10	Moderate	Negative	...	—	—	—	Bowing disappeared under sunlight
27	13	Negative	Negative	4 2	14	19	Slight	Moderate	3.5	12	11	11	Bowing disappeared after carbon arc
28	—	—	—	...	5	11	Negative	Slight	...	17	12	12	
29	—	—	—	...	5	9	Marked	Slight	...	18	18	21	Bowing persisted after rickets was cured
30	4	Moderate	Negative	...	5	10	Marked	Negative	...	14	16	16	
31	17	Moderate	Moderate	2.3	19	19	Moderate	Slight	...	14	11	20	
32	1	Negative	Negative	...	3	12	Slight	Negative	...	—	10	16	Bowing persisted in spite of egg yolk
33	—	—	—	...	5	13	Moderate	Negative	4.1	12	5	10	
34	5	Negative	Negative	...	6	13	Slight	Negative	...	—	7	15	
35	1	Negative	Negative	4.5	7	16	Marked	Moderate	2.0	—	8	10	
36	1	Slight	Negative	4.4	7	16	Moderate	Negative	...	10	3	7	
37	12	Slight	Slight	...	14	21	Slight	Moderate	2.2	13	5	8	
38	—	—	—	...	6	16	Slight	Moderate	. .	—	5	12	
39	7	Moderate	Slight	3.7	10	15	Slight	Slight	...	14	3	7	
40	—	—	—	...	2	11	Slight	Slight	...	13	17	16	Bowing disappeared under ultraviolet light

* Refers to last examination showing signs of rickets. Where rickets was absent the examination just previous to the appearance of bowing was included.

well known symptoms of this disorder. The present study has the advantage of considering craniotabes in the light of two new diagnostic criteria, roentgenologic examination of the epiphyses and the content of inorganic phosphorus in the blood.

Two hundred and eighty-nine infants have been studied for a period of many months. Of this number, sixty-eight under 4 months showed craniotabes. Only one of these sixty-eight showed rickets by roentgen-ray examination, and only one had a percentage of inorganic phosphorus within the rachitic range. In view of these findings, we are of the opinion that softening of the skull under 4 months of age is generally not the result of rickets, and is an unreliable diagnostic sign at this early period. After four months, craniotabes was intimately associated with rickets and therefore at this period should be regarded as a sign of diagnostic value.

In fourteen instances, definite bowing of the legs was observed in infants who at no time manifested clinical, roentgenologic or chemical evidences of rickets. The weight of the child and the fact that it stands early in life play a secondary rôle in the development of curvature.

A STUDY OF THE HYDROGEN-ION CONCENTRATION OF THE URINE OF INFANTS

PRELIMINARY REPORT *

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Important as is the subject of urinary acidity expressed in terms of p_H, the negative logarithm of the hydrogen-ion concentration, a survey of the literature shows that little work has been done on the urine of infants. In the few cases reported (György [1]), the determinations were made on mixed twenty-four hour specimens, and in these apparently no special precautions were taken to prevent the loss of carbon dioxid, the importance of which has been pointed out by Marshall.[2] Torres [3] worked on the titratable acidity of the urine of infants fed different levels of protein; but no p_H determinations were made.

In some work in our laboratory which included the determination of the total acidity and the ammonia content of infants' urines, it was observed frequently that the freshly voided urine was alkaline in reaction. Further investigations indicated that from time to time there was considerable variation in the reaction of infants' urines. The present study, therefore, was undertaken in an attempt to secure data concerning the normal p_H of the urine of infants who were receiving some of the usual types of artificial feeding mixtures in use in this hospital, in order to determine to what extent the various constituents of these mixtures influence the urinary acidity.

METHOD

During the observation periods, the infants were kept on a Hoobler metabolism frame, and the urines were collected at hourly intervals during the day and every two hours during the night (from 7 a.m. to 7 p.m. for the day, and from 7 p.m. to 7 a.m. for the night. When the infants did not void spontaneously, which happened very rarely, results were obtained by placing a warm pad over the bladder, or by

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* From the Department of Pediatrics, College of Medicine and the Child Welfare Research Station, State University of Iowa.

1. György, P.: Jahrb. f. Kinderh. **99**:109 (Aug.) 1922.
2. Marshall, E. K., Jr.: J. Biol Chem. **51**:3 (March) 1922.
3. Torres, C.: The Relation of the Reaction of the Urine to the Diet in Infants and Children, AM. J. DIS. CHILD. **14**:365 (Nov.) 1917.

gentle massage of the abdomen. In view of Marshall's work showing that great care must be exercised to avoid loss of carbon dioxid, the urines in the experiments reported were collected under a heavy layer of toluene after a fall through free air of less than 1 inch (2.5 cm.). At the end of the hour, the bottles were removed with as little shaking as possible to an icebox. The specimens were usually examined within a few hours.

Denis and Minot [4] found no change in the carbon dioxid content of urines preserved for twenty-four hours in chloroform in well-stoppered bottles at room temperature. We found that analysis of urines immediately after voiding, and then again after standing under toluene for an hour at room temperature showed practically no variation, at most from 0.1 to 0.2 p_H. The acid urines, kept in the icebox for twenty-four hours, also showed little or no variation for that period, but with very alkaline urines kept under the same conditions there was evidently some loss of carbon dioxid, for the acidity decreased from 0.1 to 0.4 p_H. Although in all cases recorded, determinations in general were made within a few hours after voiding, the percentage of error is probably greater in those specimens where the p_H was more alkaline than 7.2. It will be noted, however, that some of the urines, where the diet contained added alkali, reached values as low as 8.6. Marshall states that p_H 8.0 is probably the lower limit in human urines, so while in the alkaline urines here reported, the observed values are undoubtedly lower than the real values (by 0.1 to 0.4 p_H), we believe the relation between the hourly variations is approximately the same.

In the present study, determinations were made on urines of healthy infants receiving the various types of feeding in use in this hospital. In every case, unless otherwise stated, the infants were given the particular feeding mixture under investigation for at least three days before the determinations were made. During the first few observations, the method of Henderson and Palmer [5] was used, but that of Clark and Lubs [6] was finally adopted as being better suited to the volumes at hand. One drop of indicator per cubic centimeter of urine was used, and comparisons were made against standard tubes sealed with paraffin. We were unable to check the p_H of our standards electrometrically, but these were checked against the color plates in "The Determination of Hydrogen Ions" (Clark, 1920), and although our values cannot be considered absolute, we feel that the range of error is slight, and that the data obtained are of value for comparative purposes.

4. Denis, W., and Minot, A. S.: J. Biol. Chem. **34**:569 (June) 1918.
5. Henderson and Palmer: J. Biol. Chem. **13**:393, 1912.
6. Clark, W. M.: The Determination of Hydrogen Ions. Baltimore, Williams & Wilkins Co., 1920.

No determinations of carbon dioxid in the urine or blood were made in the present study.

COMMENT

The accompanying table gives the results. The data are grouped according to the type of feeding, the chief constituents of each type being listed, as well as the amount of protein ingested by the given baby. Day and night p_H determinations were averaged separately. The range, that is, the lowest and highest values obtained on single readings, is also recorded.

In determining the effect of various food factors on the urinary p_H, comparison must be made with care because of the multiplicity of factors. To avoid this, the simple milk dextrimaltose formula is taken as a basis

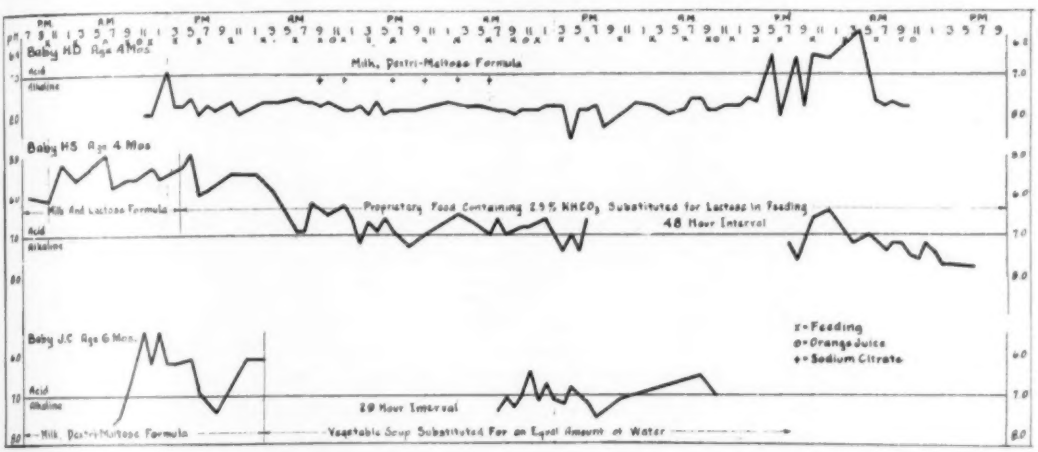

Chart 1.—The effects of alkali, alkaline proprietary food and vegetable soup on the p_H of the urine.

of comparison, and the effect of each factor determined separately by addition to or substitution in this formula.

The p_H averages of those children receiving the simple milk dextrimaltose mixtures were 6.84 for the day and 6.85 for the night. The addition of vegetable soup [7] (substituting it for part of the water of the feeding) gave urines distinctly more alkaline than those on the simple formula; substitution of a proprietary food containing 2.5 per cent. added potassium bicarbonate, for part or all of the dextrimaltose, resulted in urines still more alkaline than those on vegetable soup. This effect of added alkali is further shown by the series of curves in Chart 1 (H. S. and J. C.). Baby H. D., who was given 90 grains of sodium

7. The vegetable soup used was a concentrated water extract of turnips, carrots, celery and spinach.

Name	Age, Mo.	Method*	Type of Feeding	Protein per Kg. of Body Weight, Gm.	p_H Averages Day	p_H Averages Night	p_H Range High	p_H Range Low
							5.50	8.00
H. S.	4	C. & L.	Milk and dextrimaltose	4.2	6.90	6.57		
J. C.	6	C. & L.	Milk and dextrimaltose	3.6	6.40	6.70		
R. R.	3	C. & L.	Milk and dextrimaltose	3.8	7.06	7.10		
R. R.	3	C. & L.	Milk and dextrimaltose	3.8	6.99	7.04		
	Average				6.84	6.85		
							5.60	8.60
R. S.	7	H. & P.	Milk, dextrimaltose, vegetable soup	3.8	7.60	6.50		
R. S.	7	H. & P.	Milk, dextrimaltose, vegetable soup	3.8	7.76	7.35		
R. S.	7	H. & P.	Milk, dextrimaltose, vegetable soup	3.8	7.60	6.50		
R. S.	7	H. & P.	Milk, dextrimaltose, vegetable soup	3.8	7.37	6.85		
J. C.	6	C. & L.	Milk, dextrimaltose, vegetable soup	3.6	7.00	7.00		
H. D.	5	H. & P.	Milk, dextrimaltose, vegetable soup	3.8	7.85	8.00		
H. D.	5	H. & P.	Milk, dextrimaltose, vegetable soup	3.8	7.74	7.60		
H. D.	5	H. & P.	Milk, dextrimaltose, vegetable soup	3.8	7.73	7.70		
	Average				7.58	7.20		
H. S.	4	C & L.	Milk and proprietary food†	4.1	7.50	7.00	6.40	7.80
							7.00	8.30
R. S.	6	H. & P.	Milk, dextrimaltose, proprietary food†	3.8	7.84	7.76		
H .D.	4	H. & P.	Milk, dextrimaltose, proprietary food†	3.7	7.75	7.70		
	Average				7.80	7.73		
							5.20	7.40
H. S.	4	C. & L.	Milk and lactose	4.1	5.50	5.70		
J. C.	6	C. & L.	Milk and lactose	3.7	6.60	6.30		
J. C.	6	C. & L.	Milk and lactose	3.7	6.80	6.50		
	Average				6.30	6.20		
							5.60	7.70
J. C.	5	C. & L.	Milk, vegetable soup, dextrimaltose, lactose	3.6	6.51	6.53		
J. C.	5	C. & L.	Milk, vegetable soup, dextrimaltose, lactose	3.6	7.15	6.90		
R. R.	4	C. & L.	Milk, vegetable soup, dextrimaltose, lactose	3.7	6.74	6.65		
K. B.	5	C. & L.	Milk, vegetable soup, dextrimaltose, lactose	4.2	6.46	6.50		
	Average				6.72	6.65		
							5.60	7.90
H. S.	3	C. & L.	Goat's milk and dextrimaltose	4.4	6.70	....		
H. S.	3	C. & L.	Goat's milk and dextrimaltose	4.4	....	6.40		
R. R.	3	C. & L.	Goat's milk and dextrimaltose	3.7	6.44	6.60		
R. R.	3	C. & L.	Goat's milk and dextrimaltose	3.7	6.86	6.73		
R. R.	3	C. & L.	Goat's milk and dextrimaltose	3.7	6.63	6.97		
	Average				6.66	6.68		
							5.90	7.80
K. M.	4	C. & L.	Milk, dextrimaltose, lactic acid	7.2	7.00	6.70		
K. M.	4	C. & L.	Milk, dextrimaltose, lactic acid	7.2	7.46	6.86		
	Average				7.23	6.78		
J. C.2		H. & P.	Fermented milk and dextrimaltose	4.6	6.90	7.10	6.50	7.60
							5.40	8.60
J. C.	3	H. & P.	Fermented milk, dextrimaltose, extract wheat embryo	4.9	7.40	7.90		
J. C.	3	H. & P.	Fermented milk, dextrimaltose, extract wheat embryo	4.9	7.45	7.64		
J. C.	3	H. & P.	Fermented milk, dextrimaltose, extract wheat embryo	4.9	7.57	7.77		
J. C.	3	H. & P.	Fermented milk, dextrimaltose, extract wheat embryo	4.9	7.60	7.67		
D. U.	1	C. & L.	Fermented milk, dextrimaltose, extract wheat embryo	52	6.68	6.75		
D. U.	1	C. & L.	Fermented milk, dextrimaltose, extract wheat embryo	5.2	6.85	6.65		
D. O.	5	C. & L.	Fermented milk, dextrimaltose, extract wheat embryo	4.6	6.27	5.95		
D. O.	5	C. & L.	Fermented milk, dextrimaltose, extract wheat embryo	4.6	6.52	6.25		
	Average				7.04	7.08		
H. D.	5	H. & P.	Milk, dextrimaltose, extract wheat embryo	3.7	7.54	7.80	6.90	8.00
							5.60	7.70
W. C.	2	C. & L.	Fermented milk, dextrimaltose, lactose	2.6	6.87	6.80		
W. C.	2	C. & L.	Fermented milk, dextrimaltose, lactose	2.6	6.76	6.40		
	Average				6.82	6.60		
J. C.	2	H. & P.	Fermented milk, lactose, extract wheat embryo	4.2	6.88	7.68	6.20	7.70

* C. & L., Clark and Lubs; H. & P., Henderson and Palmer.
† Contains 2.5 per cent. potassium bicarbonate.

citrate distributed throughout twenty-four hours, shows a similar depression of the p_H. This also occurred in two other patients who were given sodium citrate. Alkali, therefore, whether given in the form of sodium citrate or in the feeding (as in proprietary foods containing added alkali) results in a definitely more alkaline urine. The addition of vegetable soup to the feeding mixture had the same effect in all patients treated.

The substitution of lactose for dextrimaltose in the simple formula resulted in distinctly acid urines in all cases. In fact, the most acid urines examined were on these mixtures, the p_H values for the day averaging 6.30 and for the night 6.20, and even though vegetable soup was used in some of the lactose mixtures, the urines continued to be acid and gave values averaging higher than those which were obtained on the milk dextrimaltose feedings. Goat's milk with dextrimaltose also resulted in consistently acid urines.

The addition of lactic acid in one patient, covering a period of forty-eight hours, resulted in more alkaline day and more acid night urines than the milk dextrimaltose formula, while the substitution of fermented milk gave very slightly more alkaline values in the one case tried. The addition of wheat embryo extract [8] to fermented milk mixtures did not markedly change the urinary p_H, although when wheat embryo extract was given to one baby in addition to the simple formula, the urines for the twenty-four hour period were more alkaline. With fermented milk feedings, as with the simple feedings, lactose seemed to increase the urinary acidity. More data on all these points are needed before conclusions can be drawn. These data are included here merely to show the range.

It will be noted that the urinary p_H values observed, ranged from 5.2 to 8.6 for the various types of feedings studied. Examination of the total number of hourly values, excluding those where alkali was given, shows that by far the largest proportion of the p_H values fell between 6.0 and 7.9.

Torres [9] determined the titratable acidity of infants' urine in its relation to the protein intake and found that when the latter was high, the urine was more acid. No p_H determinations were made. György,[10] working with the twenty-four hour specimens of infants' urine, found that the daily p_H values ranged from 5.25 to 7.70. In one case, a sick infant, aged 4½ months, on a fermented milk feeding supplying 5.05 gm. of protein per kilogram of body weight, excreted a urine in which the p_H values varied from 6.85 to 7.60 with an average of

8. Made from wheat embryo, alcohol extracted for forty-eight hours, distilled to remove alcohol, filtered and made up to volume with distilled water.

9. Torres: Footnote 3.

10. György: Footnote 1.

7.00. The urine of a healthy baby, aged 2 months, on a milk and cream and sugar formula with 3.5 gm. of protein per kilogram of body weight, had a p_H range of from 5.25 to 5.61 with an average of 5.50. Apparently, the p_H of the urine did not parallel the protein intake in this work. Similarly, our data do not show an increase of acidity with the higher protein ingestion. A comparison of the p_H values, with the protein ingested in each type of feeding, also shows no marked or consistent increase in acidity as shown by the p_H values with increase of protein. Our results, therefore, seem to indicate that protein intake is not the controlling factor in influencing the p_H of the urine.

In some cases a decided increase was observed in the acidity of the night urines. This seemed to be an individual factor, as certain infants more often showed such a rise, while in others, either there was no difference between day and night or there was a decrease in the acidity of the night urines. The three types of curves shown in Charts 2, 3 and 4 illustrate these variations. Careful records of crying spells, and periods of sleep and wakefulness were kept, but show no apparent influence on the variations in p_H.

In adults, Hubbard and Munford,[11] Hubbard, Munford, and Allen,[12] Dodds,[13] and Fiske [14] have shown that there is an "alkaline tide" following meals. In infants, so far as we have been able to find, no hour-to-hour study of the urinary p_H has been made, and therefore no "alkaline tide" has been noted. In our study, graphs recording the feedings and the p_H values of the hourly urines were made. These showed that in 57 per cent. of all the feedings given, eliminating the few cases where alkali was definitely added, there was a distinct "alkaline tide" following each feeding. In these, the drop in the p_H curve came from one to three hours after feeding. An acid rise following the "alkaline tide" was often noticeable just before the next feeding, certain children showing a definite periodicity of alkaline and acid urines as is illustrated in Chart 2. There is a possibility that the frequency of the feedings (from three to four hours) masked the "alkaline tide" in some of the other cases.

SUMMARY

In the present study, p_H determinations were made on urines obtained from healthy infants every hour during the day and every two hours during the night, care being taken in collecting and storing

11. Hubbard, R. S., and Munford, S. A.: Presence of the "Alkaline Tide," J. A. M. A. **80**:304 (Feb. 3) 1923.
12. Hubbard, R. S.; Munford, S. A., and Allen, E. G.: Am. J. Physiol. **68**:207 (April) 1924.
13. Dodds, E. C.: Brit. J. Exper. Path. **4**:13 (Feb.) 1923.
14. Fiske, C. H.: J. Biol. Chem. **49**:163 (Nov.) 1921.

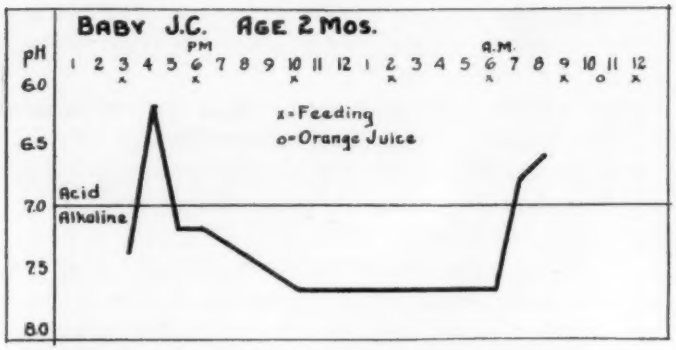

Chart 2.—The decrease in urinary acidity during the night.

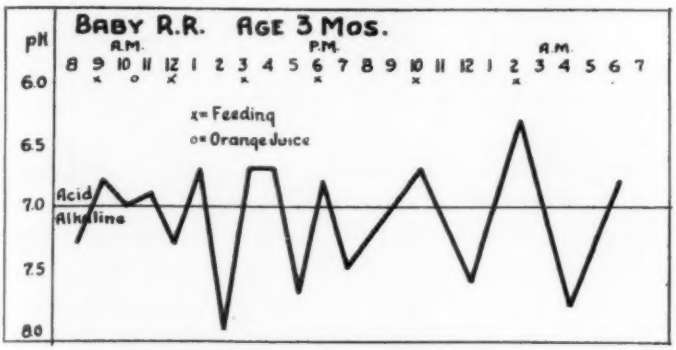

Chart 3.—Acid and alkaline tides.

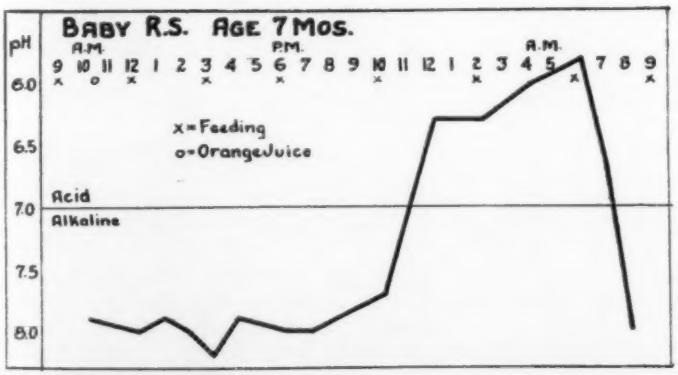

Chart 4.—Increase in urinary acidity during the night.

the specimens to avoid loss of carbon dioxid. The infants were receiving the various types of feeding formulas in use in this hospital.

1. The p_H range in the majority of cases was from 6.0 to 7.9, with extreme values of 5.2 and 8.6.

2. Using the milk dextrimaltose as a basis for comparison, it was observed that the addition of alkali, whether in the form of sodium citrate or in the feeding (as in the case of proprietary food containing added alkali) resulted in a definitely more alkaline urine. The addition of vegetable soup had a similar effect.

3. The substitution of lactose for dextrimaltose, or of goat's milk for cow's milk in the simple feeding mixture gave more acid urines.

4. The results obtained indicate that the protein intake is not the controlling factor in influencing urinary p_H.

5. An "alkaline tide" was noticeable after 57 per cent. of all feedings, excluding those to which alkali was added.

PROGRESS IN PEDIATRICS

A REVIEW OF THE LITERATURE ON SMALLPOX, VACCINATION AND CHICKENPOX, FROM JANUARY, 1923, TO OCTOBER, 1924 *

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SMALLPOX

Recent literature on smallpox is devoted largely to demonstrating that this pestilence is menacing constantly; that vaccination, properly employed, is as potent a preventive as ever. Even a casual glance at the literature suffices to show that the subject of smallpox is by no means closed.

ETIOLOGY

Conclusive proof that smallpox is due to any agent other than a filterable virus, is still lacking. Von Niessen [1] has advanced a pleomorphic bacillus ("pockenbazillus") as the etiologic factor in smallpox, an observation not confirmed by others, and denied by Gins [2] because of failure to demonstrate Guarnieri bodies. (See Footnote 17.)

Blaxall [3] found that material from smallpox patients produced no result when inoculated into the skin of calves, but a very definite and typical vesiculation when inoculated into the skin of monkeys. When the vesicular material of monkeys is passed through three calves, it produces typical vesiculation in the third calf. Monkeys inoculated with variolous material are immunized against vaccinia. Rabbits and calves exhibit immunity proportional to the extent of vesiculation produced. Vaccinated animals are immune against inoculations of variolous material.

PATHOLOGY

According to Hoffman,[4] the blood in smallpox reveals a high leukocytosis beginning at the fourth day, usually with a high eosinophilia, marked relative lymphocytosis, presence of myelocytes and an initially

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1. Von Niessen: Deutsch. med. Wchnschr. **49**:389 (March 23) 1923, and earlier articles.
2. Gins, H. A.: Deutsch. med. Wchnschr. **48**:1730 (Dec. 29) 1922.
3. Blaxall, F. R.: Bull. de l'Acad. d. méd., Paris **89**:146 (Jan. 23) 1923.
4. Hoffman, W. H.: J. Trop. Med. **26**:217 (June 15) 1923.

high Arneth index. (The differential count is the same in chickenpox, but there is no leukocytosis in the latter.) In smallpox the changes in the blood count are still marked at the end of the sixth week and probably longer. Serial blood counts in a single case of smallpox [5] confirmed the monocytosis and the myelocytic reaction.

Sheldon [6] cites from the literature a number of cases of smallpox with bone lesions, adding two of his own. The characteristic findings were destructive lesions of the epiphyses, not involving the periosteum, with resulting shortening, ankylosis and deformity. Brown and Brown [7] present a complete review of the literature, and from studies of their own conclude that there are two distinct forms of osteomyelitis complicating or following smallpox: first, the ordinary pyogenic metastatic osteomyelitis occurring in other infectious diseases; second, a distinct form of necrosing, nonsuppurating osteomyelitis, probably due to the specific virus of smallpox, frequently involving the diaphyseal ends of the long bones, destroying the epiphyseal lines and causing late deformities. The specific form of variolar osteomyelitis occurs most frequently in children. It is usually not recognized as osteomyelitis during the acute clinical stage.

Pemphigoid eruption [8] complicating and following smallpox, has also been described.

Wanklyn [9] mentions the acute fatty degeneration of the liver cells occurring early in the disease.

DIAGNOSIS

Though smallpox may well be called inexcusably common, the fact remains that the majority of physicians see so few cases of it that they dare not rely on their own ability to diagnose it. Obviously, chickenpox is the condition most likely to cause confusion. Hill [10] presents a very practical list of differential points which, for the sake of convenience, I have tabulated.

Practically all of those who have recently written on the differential diagnosis of smallpox [11] are in substantial agreement with Wanklyn [12]

5. Sabrazes, J., and Massias, C.: Arch. d. mal. du cœur **16**:777 (Nov.) 1923; abstr., J. A. M. A. **82**:339 (Jan. 26) 1924.

6. Sheldon, F. B.: Am. J. Roentgenol. **10**:35 (Jan.) 1923.

7. Brown, W. L., and Brown, C. P.: Osteomyelitis Variolosa, J. A. M. A. **81**:1414 (Oct. 27) 1923.

8. Palma, J. C., and Miyara, S.: Semana méd. **1**:133 (Jan. 17) 1924.

9. Wanklyn, W. McC.: Brit. M. J. **2**:309 (Aug. 23) 1924.

10. Hill, H. W.: Canad. M. A. J. **13**:162 (March) 1923.

11. Garrett, J. H.: Lancet **1**:1254 (June 23) 1923. McVail, J. C.: Brit. M. J. **2**:338 (Aug. 25) 1923. Hoyne, A. L.: Illinois M. J. **43**:433 (June) 1923. Painton, G. R.: Brit. M. J. **2**:1080 (Dec. 8) 1923. Rigden, G. F.: Brit. M. J. **2**:1080 (Dec. 8) 1923.

12. Wanklyn, W. McC.: Brit. M. J. **1**:464 (March 15) 1924.

in his insistence on the importance of the following diagnostic points in differentiating even the mild cases of smallpox: (1) prostration; (2) distribution on the skin; (3) localization in the skin; (4) maturation.

TABLE 1.—*Points in the Differential Diagnosis of Smallpox and Chickenpox*

SMALLPOX	CHICKENPOX
INCUBATION PERIOD	
Twelve to fourteen days from exposure to symptoms.	Two weeks to eighteen days.
PREVIOUS ATTACK	
No history. (This is unreliable. Absence of pitting is important.)	No history.
PREVIOUS VACCINATION	
No successful vaccination within five to seven years. Look for scar.	"Take" within five to seven years makes chickenpox probable diagnosis.
PRODROMES	
Marked. Lasts three full days. Headache, backache, fever, chill, epigastric pain, severe onset.	None. If present, duration not over twelve to thirty-six hours.
FIRST SIGNS OF ERUPTION	
Third or fourth day.	First few hours of illness.
ERUPTION BEGINS	
On face and wrists.	On back, chest or face.
ERUPTION MOST PROFUSE	
On limbs.	On body.
PALMS AND SOLES	
Nearly always attacked.	Seldom attacked, and if so, lightly.
ERUPTION DEVELOPS	
In one crop.	In successive crops, on successive or alternate days.
CHARACTER OF LESIONS	
Round at all stages. Margins not crenated. Four stages: 1. "Fleabite" macules, each lasting twenty-four hours. 2. "Shotty" papules, each lasting twenty-four hours. 3. Umbilicated "shotty" vesicles, each lasting from twenty-four to seventy-two hours, third to fifth day of eruption. 4. Firm opaque pustules, each lasting from four to six days, sixth to twelfth day of eruption. 5. Firm crusts about thirteenth day. 6. Dense scabs, "mahogany plaques," lasting many days.	Round and oval. Margins often crenated. Stages: 1. Macules, each lasting few hours. 2. Soft papules, each lasting few hours. 3. Thin, clear vesicles, each lasting few hours. 4. Vesicles usually destroyed before pustulation can begin. 5. Crusts of variable duration.
PITTING	
Deep and permanent if pustulation is marked. Pits are red for months and then white. Mild smallpox yields few and small pits.	Pits few and superficial, often oval.

Wanklyn [13] lists the following diagnostic criteria as obsolete and unreliable: umbilication, shottiness, presence of palatal and buccal lesions, presence of lesions on soles. Cropping and uniloculation are also often not definite.

The use of such terms as alastrim, varioloid, amaas, in describing mild smallpox has been condemned by Garrett [11] as also by Leake and Force [14] as misleading and harmful from the point of view of both

13. Wanklyn, W. McC.: Brit. M. J. **2**:106 (July 21) 1923.
14. Leake, J. P., and Force, J. N.: Smallpox and Vaccination, J. A. M. A. **81**:1072 (Sept. 29) 1923.

diagnosis and prevention. The two latter authors believe Rocky Mountain spotted fever to be essentially identical with smallpox. They emphasize the importance of clinical rather than laboratory methods of diagnosis, and note that it was a series of entirely unsuspected mild cases that gave the virulent Dresden epidemic its start. They observe further that only celerity in diagnosis and emergency vaccination keep smallpox down in the otherwise largely unvaccinated masses of London.

A number of recent articles are concerned with the mild type of smallpox and its diagnostic difficulties. Tièche [15] describes the mild cases of smallpox occurring in 1921 and 1922 in the German cantons of Switzerland where compulsory vaccination has been repealed. Pattin [16] reports a severe case of chickenpox with distribution simulating that of smallpox because of severe sunburn acquired four days previously. Esau [17] reports a case of varioliform syphilid, giving the differential diagnosis by history, clinical manifestations and serology.

It is quite possible that in some cases the leukocyte and differential blood counts already described [4] might be of assistance in differential diagnosis.

The "Paul method" [18] of diagnosis is of decided interest from the experimental point of view, though hardly susceptible of general clinical application. The method was originated by Guarnieri in 1892. He pointed out that on inoculation of the rabbit's cornea (after preceding scarification or puncture) with pustular contents of cowpox or smallpox, active proliferation of epithelial cells occurs within twenty-four to thirty-six hours. Tiny round hummocks with depressed craters appear. Within the cytoplasm of some of the affected cells are curious inclusions known as Guarnieri bodies, pathognomonic of the activity of vaccinia or variola virus. Paul first applied this method to diagnosis. According to Scott and Simon, the Paschen test (microscopic examination of vesicular contents) is less reliable, unless the worker is thoroughly familiar with it.

RESEARCHES ON VACCINE VIRUS

Thomson [19] believes that the virus of vaccinia cannot be an ordinary bacterium. His experiments convince him that the virus is not a filter passer; that the cell inclusions known as Guarnieri bodies are parasites, thus disagreeing with von Prowazek and his followers who maintain

15. Tièche: Schweiz. med. Wchnschr. **53**:448 (May 3) 1923; abstr., J. A. M. A. **81**:614 (Aug. 18) 1923.
16. Pattin, H. C.: Lancet **2**:510 (Sept. 8) 1923.
17. Esau: Med. Klin. **20**:1109 (Aug. 10) 1924.
18. Scott, J. M., and Simon, C. E.: Am. J. Hygiene **3**:401 (July) 1923.
19. Thomson, D.: Ann. "Pickett-Thomson Research Laboratory," London **1**:1 (July) 1924.

that these bodies represent a cell reaction around an infective granule. He believes that the problem cannot be solved until the Guarnieri bodies can be cultivated in large numbers, and until they can be proved to be infective and capable of producing vesicles in susceptible animals.

Lucksch [20] found no difference between the keratitis produced in rabbits by cowpox lymph and that produced by the contents of herpes vesicles. The degeneration of cells in herpes resembled Guarnieri bodies perfectly.

With regard to the potency of vaccine virus, Illert [21] notes large individual differences in rabbits tested with vaccine. In his opinion, tests on man are necessary if the value of lymph is to be determined. From experiments with rabbits, Bachmann and Biglieri [22] conclude that the protection conferred by vaccination with one strain of vaccine virus is not always complete against the virus of another strain.

The time drop method [23] of measuring surface tension reveals the amount of antibodies contained, but it is not specific. Tests of rabbit serum diluted 1 : 10,000 made thirteen days after vaccination, revealed a uniform increase of about 10 dynes (from 65 to 75).

Von Einsiedel [24] discusses the antitoxic or antigenic results of an attack of smallpox, and the manner of formation of humoral immunity.

Levaditi and Nicolau [25] obtained a virus which, when inoculated into rabbits' brains, produced death in five or six days. The brain, in glycerinated emulsion ("neurovaccine") constituted a vaccinal pulp free from all organisms. According to Levaditi [26] his "vaccine ultravirus" has specific affinity for tissues derived from ectoderm and for some organs of endodermal origin, practically no affinity for mesodermal tissues or for blood. (Compare Levaditi's neurotropic spirochete of general paresis and tabes.)

From a commercial sample of "neurovaccine," Camus [27] concludes that the product is worthy of study, but for the present should not be tried on human subjects. He found the percentage of positive takes in unvaccinated infants to be 77 instead of the 99 when ordinary vaccine

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20. Lucksch, F.: Med. Klin. **20**:1170 (Aug. 17) 1924; abstr., J. A. M. A. **83**:1040 (Sept. 27) 1924.
21. Illert, E.: Deutsch. med. Wchnschr. **49**:446 (April 6) 1923; abstr., J. A. M. A. **81**:172 (July 14) 1923.
22. Bachmann, A., and Biglieri, R.: Rev. Soc. méd. arg. **35**:947 (Dec.) 1922; abstr., J. A. M. A. **80**:1740 (June 9) 1923.
23. Du Nouy, P. L.: J. Exper. Med. **37**:659, 1923; ibid. **40**:129 (July) 1924.
24. Von Einsiedel: Med. Klin. **20**:441 (April 6) 1924.
25. Levaditi, C., and Nicolau: Compt. rend. Acad. d. sc. (Jan. 22) 1922.
26. Levaditi, C.: J. State Med. **32**:151 (April) 1924; abstr., J. A. M. A. **82**:1734 (May 24) 1924.
27. Camus, L.: Bull. de l'Acad. d. méd., Paris **90**:79 (July 19) 1923.

is used. The sterility of cultures of this preparation he believes to be an unnecessary advantage. He considers the likelihood of severe reactions to be strong. Roux, in his discussion of Camus' paper, considers Levaditi's observations to be of more scientific than practical importance. The suggested possibility of a relation between the embryonal origin of certain tissues and the microbic diseases of which these tissues are the seat, is very important, especially in the light of poliomyelitis and herpes viruses. Marie [28] obtained 43 per cent. successful (typical pustular) "takes" and no severe reactions.

Anemia in infants [29] apparently does not alter the response of the blood and temperature to vaccination. It is no contra-indication to vaccination.

METHODS OF VACCINATING AND OF RECORDING RESULTS

As a vehicle for vaccine lymph in the tropics, glycerin has been shown,[30] to be preferable to hydrous wool fat. The interdermal method of vaccination has been recommended by a number of observers,[31] because of the absence of severe reactions, of secondary infection and of scar formation. The absence of a scar of course obliges us to take the physician's or the patient's word for a successful take. (See Footnote 51.)

As Leake [32] remarks, vaccination protects against smallpox and against itself. The latter is evidenced by alteration in the course of a vaccination take, produced by previous vaccination. He thus describes the normal course of primary vaccination: after three days, slight redness over an area of 1 or 2 mm.; from five to seven days, grayish vesicle or pustule. Rapid spread of red area begins; from eight to eleven days, widest spread of red zone.

He records as "vaccinoid" an acceleration and diminution in severity of the same course. He records as "immunity reaction" the rapid production of the first stage of the process without vesicle or true area formation, the redness and induration being greatest from twelve to seventy-two hours after inoculation. This reaction varies with persons and with the potency of the virus. Leake notes that the "green virus" advocated by Gins is used without artificial reduction of bacterial con-

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28. Marie, A.: Bull. de l'Acad. de méd., Paris **90**:123 (July 31) 1923.

29. Thomas, E., and Schäfer, M.: Monatschr. f. Kinderh. **28**:454 (Aug.) 1924; abstr., J. A. M. A. **83**:1115 (Oct. 4) 1924.

30. Cunningham, J., and Cruickshank, J. A.: Indian J. M. Res. **11**:1173 (April) 1924.

31. Berney, D. E.: Atlantic M. J. **27**:713 (Aug.) 1924. Singer, A.: Med. Klin. **19**:1288 (Sept. 23) 1923. Fitzsimmons, A. P.: Nebraska M. J. **9**:148 (April) 1924. Starkey, F. R.: J. Mich. M. S. **23**:70 (Feb.) 1924. Frankenstein, C.: Deutsch. med. Wchnschr. **48**:1700 (Dec. 22) 1922.

32. Leake, J. P.: Mil. Surgeon **53**:328 (Oct.) 1923.

tent, as by glycerination and storage. Takes are more severe when this virus is used. Glycerination out of cold storage is detrimental to virus. The protection afforded by vaccination against smallpox is greater than that against vaccinia. The protection against hemorrhagic smallpox, even by recent vaccination, is less than that against the discrete or confluent variety. Leake further emphasizes that immunity to smallpox is slower in becoming established than is commonly supposed. The vaccination must be performed prior to exposure, and the acme of the reaction reached and passed, if protection is to be counted on. The duration of immunity is apparently shorter in the negro.

In discussing vaccination and quarantine, Grubbs [33] says that contacts showing an immune reaction in less than forty-eight hours may be released from quarantine. If the reaction occurs after forty-eight hours, immunity is not complete, and smallpox may develop in a mild form. These persons must be held ten days after vaccination.

As an example of what may be accomplished by thoroughness, Abeken,[34] reporting results obtained on board the U. S. S. *Mississippi,* obtained 100 per cent. positive reactions in 3,848 vaccinations (96.2 per cent. gave reaction of immunity, 2.5 per cent. "vaccinoid," (1.3 per cent. vaccinia). The routine for negative reactions consisted of a series of three vaccinations (drill method) every six months until a positive reaction was obtained.

PREVALENCE OF SMALLPOX

As recently as Oct. 25, 1924,[35] *The Journal of the American Medical Association* reports that during the first six months of this year, in 678 cities of the United States and Canada there were 18,811 cases of smallpox, with 242 deaths. Last year and the year before there were 7,170 and 7,355 cases during the same period. The disease is nationwide this fall.[36]

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33. Grubbs, S. B.: Pub. Health Rep. **38**:2201 (Sept. 21) 1923.
34. Abeken, F. G.: U. S. Nav. M. Bull. **18**:79 (Jan.) 1923.
35. General News, J. A. M. A. **83**:1344 (Oct. 25) 1924.
36. Only a few of the small epidemics noted in the news column of *The Journal of the American Medical Association* are listed, merely as examples: "State of epidemic" in the City of Amsterdam, N. Y., Oct. 3., J. A. M. A. **83**:1174 (Oct. 11) 1924. Opening of Norwood (W. Va.) school delayed one week beginning September 8 on account of smallpox, ibid., p. 1175. Smallpox in State Asylum, Austin, Texas, J. A. M. A. **83**:1253 (Oct. 18) 1924. Smallpox at Sidney, Mont. (mostly children), J. A. M. A. **83**:1252 (Oct. 18) 1924. Six cases smallpox at Leggett School, Akron, O., Sept. 27, 1924, J. A. M. A. **83**:1253 (Oct. 18) 1924. Smallpox in Michigan and Canada. During the first six months of 1924, 3,999 cases of smallpox were reported in Michigan. Of these, 1,532 were in Detroit and 2,513 in the rest of the state. There were 106 deaths in Detroit during this period, and twenty-seven in the rest of the state, J. A. M. A. **83**:129 (July 12) 1924.

VIRULENCE

Heiser [37] gives the statistics in Table 2 for smallpox cases and deaths in 246 American cities.

TABLE 2.—*Statistics for Smallpox Cases and Deaths in Two Hundred and Forty-Six American Cities*

	1920	1921	1922
Total cases	27,775	25,514	8,306
Total deaths	177	298	475
Case fatality, per cent	0.6	1.2	5.7

The U. S. Public Health Reports [38] also indicate a decided increase in the virulence of smallpox in the United States during recent epidemics, for example, in Kansas City (both Kansas and Missouri) in the late summer of 1921, and in Denver in the autumn of 1921 through the winter of 1922. There were 660 cases in Denver in 1922, with 226 deaths. Reports of health officers of 275 cities of the United States and Canada [39] show that the case-fatality-rate for smallpox in 1922 was five times the rate for 1921 (this agrees with Heiser's figures). Similar figures from other parts of the United States are given in the articles listed below.[40]

In England in 1922 there were two different epidemics,[3] one in London and vicinity, affecting only a few, but of great virulence and with high mortality; the other in central and northern England, with 821 cases reported for the year, practically all mild, with only three deaths, two of these in unvaccinated infants, the third in an adult vaccinated thirty-two years previously. In the London epidemic there were seventy-four cases, with twenty-four deaths.

In 1924, there has been another marked increase in the number of cases of smallpox in England and Wales,[41] the total up to mid-September being 2,750 (1,840 in the corresponding period of 1923). Though the cases for the most part have been mild, severe ones have occurred from time to time.

As an illustration of the rôle which mild cases may play in the spread of this disease, we may consider the outbreak of "alastrim" in Antigua,

37. Heiser, V. G.: Menace of the Unvaccinated, J. A. M. A. **81**:1070 (Sept. 29) 1923.

38. Pub. Health Rep. **38**:1406 (June 22) 1923.

39. Statistical Bull. Metropolitan Life Ins. Co., April, 1923.

40. Illinois: Last year one death among each 200 cases, this year nearly three deaths in 200 cases, J. A. M. A. **83**:1172 (Oct. 11) 1924. New Orleans: 1917, 173 cases, no deaths; 1918, 207 cases, no deaths; 1919, 104 cases, three deaths.

41. London Letter, J. A. M. A. **83**:1091 (Oct. 4) 1924.

B. W. I.[42] This epidemic was traced to a woman who concealed the disease, who presented a certificate of successful vaccination, but had no scar. The epidemic was quickly controlled by vaccination.

PREVENTION OF SMALLPOX

Historical.—A number of articles on the history of smallpox and its control have appeared and are listed by title. Lack of space prevents abstracting them.[43]

VACCINATION AND THE CONTROL OF EPIDEMICS OF SMALLPOX

Though all physicians are of course agreed on the efficacy of vaccination, the manner of its application to certain communities is still debated. Olson (quoted by Gage[44]) argues that if all cases of smallpox were "unquarantined," with the full knowledge of all citizens; and if the citizens were kept aware that complete protection by vaccination is at all times available, the citizens themselves would lead the fight for a clean community, and the element of compulsion would be removed. Stuver[45] notes that this idea dates back to 1911. The editorial comment on his letter, however, calls attention to the fact that in spite of the laxity of the vaccination laws of Minnesota, this state has had as bitter an antivaccination fight as has been waged elsewhere, with correspondingly high morbidity from smallpox.

Another, and essentially opposite view of vaccination is that of Millard,[46] who, in stressing the power of vaccination to protect the

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42. Branch, E. W. R., and McDonald, W. M.: J. Trop. Med. **26**:214 (June 15) 1923. Naegeli: Epidemic of Mild Smallpox in Switzerland, 1921-1923, Schweiz. med. Wchnschr. **53**:461 (May 10) 1923; abstr., J. A. M. A. **81**:786 (Sept. 1) 1923.

43. Mariscal, N.: History of Vaccination (Jenner Centennial), Siglo méd. **71**:329 (April 7) 1923. Lendon, A. A.: Jenner, 1749-1823, M. J. Australia **2**:535 (Nov. 24) 1923. Millard, C. K.: Smallpox, Jenner and Vaccination, J. State Med. **31**:416 (Sept.) 1923. Chauffard, A.: Hundredth Anniversary of Jenner's Death, Bull. de l'Acad. de méd., Paris **89**:85 (Jan. 23) 1923. Camus, M. L.: Jenner and Vaccination, Bull. de l'Acad. de méd., Paris **89**:89 (Jan. 23) 1923. Von Liebermann, L.: Goethe and Compulsory Vaccination, Deutsch. med. Wchnschr. **49**:557 (April 27) 1923. Torkomian, V.: History of Inoculation Against Smallpox in Armenia, Bull. de l'Acad. de méd., Paris **90**:108 (July 24) 1923. Miyajima, M.: History of Vaccination in Japan, Proc. Roy. Soc. med. **16**:23 (Sept.) 1923. Gins, H. A.: History of Smallpox Vaccination, Klin. Wchnschr. **3**:634 (April 1) 1924. Gimeno, A.: Balmis' Vaccination Mission, Siglo méd. **71**:453 (May 12) 1923. d'Espine, A.: Rôle of Doctors in Geneva in Propagating Vaccination, Bull. de l'Acad. de méd., Paris **89**:141 (Jan. 23) 1923. Tandy, E. C.: Local Quarantine and Inoculation for Smallpox in American Colonies, Am. J. Pub. Health **13**:203 (March) 1923.

44. Gage, W. V.: Shall the Public Take Full Responsibility for Smallpox? J. A. M. A. **83**:941 (Sept. 20) 1924.

45. Stuver, E.: "Shall the Public Take Full Responsibility for Smallpox?" J. A. M. A. **83**:1186 (Oct. 11) 1924.

46. Millard, C. K.: Brit. M. J. **2**:313 (Aug. 23) 1924.

person, maintains that its power to protect a community has been overestimated. He deplores reliance on infant vaccination for protecting a community, maintaining in this as in other articles [47] that infant vaccination encourages the spread of smallpox by making the disease so mild as often to mask its true nature. He relies mainly on isolation and general sanitary measures, together with thorough recent vaccination of a community in the event of a threatened epidemic.

Wanklyn [9] opposes this idea with the contention that mild cases of smallpox do not always "breed true," citing instances of severe cases due to contact with mild ones, as in Detroit. (See also Leake and Force,[14] Tièche.[15].) Garrett [11] opposes it with the fact that many unvaccinated children had the mild smallpox which was epidemic in Yorkshire and Derbyshire. It is interesting to note, however, that in Antigua, the epidemic of mild smallpox which has already been mentioned,[42] infant vaccination is compulsory.

As might be expected, the great majority of recent articles on this phase of the subject of smallpox are concerned more with the relation between the incidence of smallpox and the extent of community vaccination.

Gins [48] says that systematic vaccination has changed smallpox from a disease of children to a disease of old people. From 1758 to 1774, 98.7 per cent. of the smallpox deaths occurred in children under 12. In 1916 to 1917, 90.56 per cent. occurred in people over 40.

Guilford,[49] in an article primarily for laymen, asserts, "The discovery of smallpox vaccination by Edward Jenner is possibly the greatest blessing ever to come upon mankind." He reminds us—and in these days we need thus to be reminded—that in the days of Louis XV, 30,000 people died annually in France from smallpox. As recently as in 1877, Milwaukee had 1,313 cases of smallpox reported (probably half the total) with 385 deaths. In 1923, with more complete vaccination, there were sixty-nine cases and no deaths. He mentions the interesting fact that in Hometon, England, during an outbreak of smallpox, ninety-eight of the 100 attendants had been recently vaccinated. All of these escaped, and two unvaccinated attendants contracted the disease. In the thoroughly vaccinated American army, of 4,128,000, there were only fourteen deaths from smallpox. According to Guilford, it is the unprotected person who keeps the disease alive and spreading. Woodward,[50] urging compulsory vaccination of private as well as of public schoolchildren, presents similar statistics and opinions.

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47. Millard, C. K.: Brit. M. J. **2**:564 (Sept. 29) 1923; Lancet **1**:301 (Feb. 9) 1924.
48. Gins, H. A.: Med. Klin. **18**:1483 (Nov. 19) 1923.
49. Guilford, H. M.: Wisconsin M. J. **22**:521 (April) 1924.
50. Woodward, S. B.: Boston M. & S. J. **188**:309 (March 8) 1923.

In a general article on the menace of the unvaccinated, Heiser [50] gives figures for the Denver epidemic, September, 1921, to November, 1922.

TABLE 3.—*Figures for Denver Smallpox Epidemic*

	Unvaccinated	Partially Vaccinated	Vaccinated
Number of deaths	110	13	0
Percentage of total	89.4	10.6	0

He notes that prior to the American occupation, the Philippines had 40,000 deaths a year from smallpox. Thorough vaccination reduced this to practically none. Later a large number of babies were allowed to remain unvaccinated. In 1918, as a result, there was an epidemic with 50,000 deaths, halted only when advance vaccination was resorted to. Lessened vaccination due to the war resulted in similar experiences in Germany and Bulgaria. Heiser also cites rapid control of smallpox by advance vaccination in Porto Rico, Cuba and Jamaica. He adds that modern methods have made vaccination a safe process. Among 10,000,000 vaccinations in the Philippines, no injury to health by vaccination was demonstrable.

Sharpley [51] describes the type of the disease in the Denver epidemic as the most malignant that has ever appeared in this country, the mortality being a little over 30 per cent. In fourteen months, over 200,000 were vaccinated. In accepting evidence of vaccination, no method was recognized which did not show a scar.

The epidemic in Monroe County, Michigan, is reported by Ramsey.[52] It lasted from Nov. 1, 1922, to Feb. 15, 1923. Four hundred forty-nine cases were reported, 11.4 per cent. in children under 5 (which illustrates the need for early vaccination). When the State Department of Health took charge of the county's activities, the motion pictures, newspapers and all agencies of publicity pushed the vaccination campaign. An experienced law enforcement officer was of great assistance. Violators of quarantine were convicted and fined. The epidemic ceased abruptly two weeks after 50 per cent. of the city's population had been vaccinated. No new cases were reported during the following seven months.

The virulent epidemic in Windsor [53] was traced to an unvaccinated man who died of undiagnosed hemorrhagic smallpox. The real nature of his disease was not apparent until those who were in contact with him came down with recognizable smallpox. Sixty-seven cases appeared in Amherstberg, Maidstone and Detroit, with thirty-two deaths. Ninety-

51. Sharpley, W. H.: Am. J. Pub. Health **13**:222 (March) 1923.
52. Ramsey, G. H.: Am. J. Pub. Health **13**:1023 (Dec.) 1923.
53. Adams, F.: Canad. M. A. J. **14**:692 (Aug.) 1924.

five per cent. of the population of the border municipalities were vaccinated within the next six days. No one who had ever been successfully vaccinated died. Of the unvaccinated persons contracting the disease, 71 per cent. died, and those who recovered had the disease in terrible form. None of those caring for these virulent cases contracted the disease. (All had been recently vaccinated.)

It would be tedious to multiply reported statistics of this kind, which indicate so conclusively that successful vaccination within five years positively prevents smallpox; that successful vaccination at any time insures almost as definitely that the disease if contracted will not be fatal; that prompt vaccination of whole populations definitely checks epidemics.[54]

Though the obstacles to the control of smallpox in the United States and Europe are many, they are far more formidable in the Orient. In the Philippines in 1918 and 1919, after a four year period of near freedom from the disease, an epidemic occurred in which 60,447 died.[55] In 1919 in the provinces, 288 emergency hospitals, including 100 isolation houses were established. In these there were 28 per cent. of deaths, as against 54 per cent. in cases treated at home. Of 989 deaths, only sixty had ever been successfully vaccinated. There were one doctor and one nurse to every 8,000 population. Almost insurmountable difficulties were: incompleteness of notification; inadequate personnel; hostility on the part of the natives due to ignorance and superstition; large proportion of inert virus, due to heat encountered in transportation; native officers' reporting many thousands as successfully vaccinated who had really never been vaccinated; inadequate inspection of vaccinations. The report for 1921 shows the disease practically absent in Manila, and only three or four hundred cases in the provinces.

In 1922 [56] the incidence of smallpox in the Philippines was negligible. Sixty-one per cent. of the cases occurring in 1921 were in children, the majority of whom were unvaccinated or unsuccessfully vaccinated.

In 1875, Japan [57] passed regulations compelling vaccination of the new-born, also revaccination between the ages of 5 and 7, regulations which would be highly effective if enforced, as apparently they are not

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54. Dodson, J. M.: Vaccination Against Smallpox: Another Proof of Its Power, Hygeia **2**:592 (Sept.) 1924. Dewar, R. K.: Canad. M. A. J. **14**:625 (July) 1924. Pub. Health Rep. **38**:2723 (Nov. 16) 1923. Teissier, P.: Bull. de l'Acad. de méd., Paris **89**:111 (Jan. 23) 1923. (In this article it is noted that in the whole French army during the World War, there were only twenty-six cases of smallpox, most of these being in unvaccinated imported soldiers.) Camus, L.: Bull. de l'Acad. de méd., Paris **90**:439 (Dec. 4) 1923. Armand, J.: Bull. de l'Acad. de méd., Paris **89**:69 (Jan. 16) 1923.

55. McVail, J. C.: Brit. M. J. **1**:158 (Jan. 27) 1923; ibid. **2**:421 (Sept. 8) 1923.

56. Padua, R. G.: Efficacy of Antivariolar Vaccination in the Philippines During 1921 and 1922, J. A. M. A. **80**:1361 (May 12) 1923.

57. Vaccination in Japan, J. A. M. A. **81**:1102 (Sept. 29) 1923.

Discussing vaccination in French, English and Dutch colonies in the Orient, Jeanselme [58] urges, besides compulsory vaccination, the abolition of "variolization" (intentional inoculation with smallpox virus), a practice long common in the Orient. He mentions the work of the French in providing "institutes" where potent vaccine virus can be obtained. In Indo-China, for example, 3,000,000 people were vaccinated by means of these agencies in 1918.

VACCINIA AND ITS SEQUELS

The effect of tumors on the virus of vaccinia is discussed by Levaditi and Nicolau.[59] The embryonic origin of the tumor determines whether or not the virus is to be destroyed. Sarcomas kill it more or less completely.

An interesting postvaccinal cutaneous reaction is that of a woman, aged 22, reported by Templeton.[60] She was vaccinated by a nurse, without the author's knowledge. Two days later, at her request, a number of moles were removed by fulguration, from her face and neck. In a few days, the vaccination and the fulgurated moles all "took" simultaneously.

Kite [61] reports the case of a youth, aged 18, never previously vaccinated, who had an ulcer on his chin and swelling of his neck quite typical of anthrax. He had rubbed a "fever blister" on his chin with vaseline which his sisters, unknown to him, had used in rubbing their "taking" vaccinations.

In the case of a teacher, aged 50,[62] vaccination was apparently responsible for precipitating an attack of purpura. On the day of vaccination, apical dental infections were found. He had had six attacks of purpura previously.

The subject of varioliform eruptions after vaccination is exhaustively reviewed by Drago.[63]

MEDICOLEGAL ASPECTS OF SMALLPOX AND VACCINATION

Practically everywhere in the civilized world, the police power vested in boards of health for the enforcement of quarantine measures applies with greatest force when smallpox is declared epidemic. An interesting legal contest over smallpox was that of a patient [64] who

58. Jeanselme, E.: Bull. de l'Acad. de méd., Paris **89**:128 (Jan. 23) 1923.
59. Levaditi, C., and Nicolau, S.: Ann. de l'Inst. Pasteur **37**:443 (May) 1923; abstr., J. A. M. A. **81**:694 (Aug. 25) 1923.
60. Templeton, H. J.: Postvaccinal Cutaneous Reactions, J. A. M. A. **81**: 2115 (Dec. 22) 1923.
61. Kite, J. H.: J. M. A. Georgia **12**:200 (May) 1923.
62. Traut, E. F.: Illinois M. J. **44**:35 (July) 1923.
63. Drago, A.: Pediatria **32**:740 (June 15) 1924.
64. Ketcham, D.: Mod. Hosp. **21**:303 (Sept.) 1923.

underwent an operation in a hospital March 1, went home March 6, had high fever March 14, typical smallpox March 18 and died April 1. There was no exposure to smallpox except to a probable, undiagnosed case in the hospital. As there was no proof of knowledge of its existence in the hospital, the institution was not held responsible by the court.

With regard to vaccination and the law, Tobey [65] concludes his interesting discussion with a list of court decisions. He says that like all laws coming under the police power, a valid vaccination law must be reasonable. To require that any one at any time could be seized and forced to undergo vaccination would be held unreasonable by most state courts. But to require that, during an epidemic or threatened epidemic, all persons who had been exposed or reliably suspected of exposure should either submit to vaccination or be quarantined, would be entirely reasonable and upheld practically by all courts.

With regard to exclusion of unvaccinated children from school, there is some conflict in the decisions. The weight of authority, however, upholds as a valid exercise of the police power the requirement that children be vaccinated before attending school, and that they be excluded from school if not so vaccinated. A decision of the Superior Court of Cook County is an example of this.[66]

ACTIVITIES OF THE ANTIVACCINATIONISTS

Unfortunately, this review would not be complete without at least some mention of the efforts of these people who (to us) are so obviously misguided. There are two varieties of them: (1) the ignorant and sentimental, (2) far more malicious and effective, the paid propagandists, such as those who work for the Macfadden publications and the American Medical Liberty League.

Though there are many instances of the actual spread of smallpox by the "antis," such as chiropractors and the Eddyites (in California and Colorado, certain of the former carried the disease to others and died of it themselves), this fact does not prevent the gullible from giving them support. When smallpox appears, however, "antis" of this sort are likely to be conspicuous by their absence: "leaving their victims to be cared for by those who believe in vaccination" (Heiser [37]). Adams [58] found the same to be true in the Windsor epidemic.* In Denver, the business interests, anxious that the epidemic should cause no loss of trade, joined with the chiropractors and the American Medical Liberty League in opposing vaccination. When the papers began publishing the

65. Tobey, J. A.: Vaccination and the Courts, J. A. M. A. **83**:462 (Aug. 9) 1924.

66. White, B.: Boston M. & S. J. **188**:523 (April 12) 1923, quoted from: Court Rules on Vaccination, J. A. M. A. **78**:300 (Jan. 28) 1922.

names and addresses of those who died of smallpox, and noting whether or not they had been vaccinated, one and all flocked to be vaccinated.

Beatty [67] gives a particularly unfortunate example of the veniality of certain newspapers of Salt Lake City, in their refusal to publish photographs of severe cases of smallpox as propaganda, because of the certainty of punishment by their advertisers. In this epidemic the Christian scientists and chiropractors threatened to boycott motion picture theaters showing smallpox pictures and statistics. The legislators of Utah were scared into having themselves vaccinated, but, for political reasons would not repeal the existing law, and Utah is still unvaccinated.[68]

In Tunis,[69] opposition to vaccination might be expected among the Mohammedans, whose Prophet said, "There is no disease." But they apply the Mohammedan law, "The lesser of two evils is to be chosen," and submit to vaccination if performed by physicians.

An example of the more sinister misrepresentations to which "antis" resort is that by a "prominent physician," etc., named Katzoff, found, as might be expected, in "Physical Culture." [70] He reports "one of the most beautiful children he has ever known," who was vaccinated, grew rapidly weaker and died. (Though the death certificate showed that the child died of pneumonia, Katzoff is certain it was the vaccination.) Similar information, such as: "Surgery and vaccine are taking the lives of prominent people" comes from one Mrs. Lora C. Little of the American Medical Liberty League.[71]

Such activities indicate clearly how we may save life through counter-propaganda and active interest in medical legislation.

CHICKENPOX

Experiments on Transmission.—From a series of experiments on the susceptibility of rabbits to the virus of chickenpox, Rivers and Tillett [72] conclude that as the localization of the virus of chickenpox is influenced by irritation, this is indirect evidence that the virus is in the blood. Rabbits are susceptible to a virus recovered from the blood of patients with chickenpox. Testicular emulsions containing the virus produce lesions in the cornea, skin and testes of rabbits. The virus can be transmitted indefinitely from rabbit to rabbit by testicular inoculation,

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67. Beatty, T. B.: Discussion of Paper of Leake and Force, footnote 14.
68. S. W. Med. **7**:334 (Sept.) 1923.
69. Dinguizli: Bull. de l'Acad. de méd., Paris **90**:300 (Nov. 6) 1923; abstr., J. A. M. A. **82**:163 (Jan. 12) 1923.
70. "Killed by Vaccination," J. A. M. A. **82**:552 (Feb. 16) 1924.
71. The American Medical Liberty League, J. A. M. A. **79**:395 (July 29) 1922.
72. Rivers, T. M., and Tillett, W. S.: J. Exper. Med. **38**:673 (Dec.) 1923.

and can be preserved for twenty-nine days in 50 per cent. glycerol at low temperature. A virus studied by these authors [73] (virus III) behaved like a "fixed virus," constantly producing fever and skin reactions, and definite immunity in rabbits. A study of the immune reactions of virus III failed to show that it had any etiologic relation to chickenpox. Tezner [74] injected the contents of a chickenpox pustule into the spinal cord of a rabbit. The rabbit died in seventeen days with symptoms of meningitis. Cultures were negative. An emulsion of the cord produced a similar condition in another animal.

CLINICAL OBSERVATIONS

The tendency of the eruption of chickenpox to appear on sites previously irritated has already been mentioned (Wanklyn,[12] Pattin,[16] Rivers and Tillett [73]). In this connection, Dreyer [75] reports the case of a child, aged 9, who had typical chickenpox two weeks after an injury to his left knee. There was a marked accumulation of vesicles in this location. In the patient, aged 7 months, of Tillett and Rivers [76] the chickenpox rash was atypically distributed over the face, scalp and extremities, due to a preceding heredosyphilitic eruption. There were other clinical and serologic evidences of syphilis.

THE PREVENTION OF CHICKENPOX

From careful hospital observation, Harries [77] concludes that isolation in bed cannot replace small separate wards for nursing measles and chickenpox in their earlier stages.

Preventive vaccination with material from chickenpox vesicles is satisfactory, according to Soldin,[78] provided the following conditions are fulfilled: inoculation must be done early and with fresh material; children thus vaccinated must be regarded as infectious, and isolated until the expiration of the incubation period. (Reaction to the inoculation is a very mild varicella.)

Knoepfelmacher [79] recounts further experience with this process of "varicellization." He finds reinoculation negative in varicellized children, as in those who have had chickenpox in the ordinary way.

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73. Rivers, T. M., and Tillett, W. S.: J. Exper. Med. **39**:777 (June) 1924; ibid. **40**:281 (Sept.) 1924.
74. Tezner, O.: Monatschr. f. Kinderh. **28**:39 (April) 1924; abstr., J. A. M. A. **83**:75 (July 5) 1924.
75. Dreyer: Deutsch. med. Wchnschr. **50**:280 (Feb. 29) 1924.
76. Tillett, W. S., and Rivers, T. M.: Bull. Johns Hopkins Hosp. **35**:157 (May) 1924.
77. Harries, E. H. R.: Lancet **1**:491 (March 8) 1924.
78. Soldin, M.: Med. Klin. **19**:579 (April 29) 1923.
79. Knoepfelmacher, W.: Monatschr. f. Kinderh. **25**:367 (March) 1923.

Blackfan et al.[80] found that of forty-two susceptible patients treated within five days of exposure, with 5 c.c. of convalescents' serum, seven contracted the disease, and all of these were mild with relatively few lesions. Thus an efficient temporary immunity is conferred, of great value in checking hospital epidemics. Schmidt,[81] however, was unable to prevent chickenpox by injecting from 7.5 to 8 c.c. of convalescents' serum during the incubation period.

Using serum from children in whom chickenpox had developed from ten to twenty days previously, Weech[82] gave from 3 to 4.5 c.c. to each of nine exposed infants. Only one contracted the disease, and in that one the attack was very mild, occurring after an incubation period of twenty-two days.

RELATION BETWEEN HERPES AND CHICKENPOX

Experimental Work.—With antigen made from chickenpox crusts from three children, and with blood from three other children with chickenpox and from two with herpes and two controls, de Lange[83] obtained specific complement-fixation reactions. This, she believes, indicates the identity of certain cases of herpes zoster and chickenpox. Netter[84] obtained similar results, and believes the connection between herpes zoster and chickenpox is as certain as that between vaccinia and smallpox.[85]

Netter[86] has compiled sixty-nine cases of herpes zoster for which chickenpox seems to be responsible, or vice versa, and in this article tabulates seventy-two additional cases. The same virus seems to be able to induce herpes zoster and chickenpox at will, changing arbitrarily at brief intervals.

To cite only one example of this sort of cross infection, let us take that of a boy, aged 10,[87] who developed typical chickenpox. Twenty-four

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80. Blackfan, K. D.; Peterson, M. F., and Conroy, F. C.: Ohio State M. J. **19**:97 (Feb.) 1923.

81. Schmidt, W.: Med. Klin. **20**:642 (May 11) 1924; abstr., J. A. M. A. **82**:2092 (June 21) 1924.

82. Weech, A. A.: The Prophylaxis of Varicella with Convalescents' Serum, J. A. M. A. **82**:1245 (April 19) 1924.

83. De Lange, C.: Klin. Wchnschr. **2**:879 (May 7) 1923; abstr., J. A. M. A. **81**:867 (Sept. 8) 1923. See also de Lange, C.: Nederlandsch Tijdschr. v. Geneesk. **1**:1634 (April 21) 1923; abstr., J. A. M. A. **81**:260 (July 21) 1923.

84. Netter, A.: Paris méd. **1**:521 (June 7) 1924; abstr., J. A. M. A. **83**:226 (July 19) 1924.

85. Netter, A., and Urbain, A.: Compt. rend. Soc. de biol. **90**:461 (Feb. 29) 1924; Further Research on Herpes Zoster, J. A. M. A. **82**:1614 (May 17) 1924.

86. Netter, A.: Bull. de l'Acad. de méd., Paris **91**:494 (April 22) 1924; abstr., J. A. M. A. **82**:2087 (June 21) 1924. See also Netter, A., and Vallat: Bull. et mém. Soc. méd. d. hôp. de Paris **47**:874 (June 15) 1923.

87. Baur, J., and Kuntzler, C.: Bull. et mém. Soc. méd. d. hôp. de Paris **47**:1480 (Nov. 9) 1923.

days prior to the onset, his grandfather, aged 66, had had herpes zoster involving the seventh interspace. The child had slept with his grandfather in spite of this. They lived in the country, and there was no known contact with chickenpox.[88]

Condat [89] discusses the alleged proofs of the identity of herpes and chickenpox, and finds them unconvincing. Vaglio [90] considers the question still open, adding that until further light is thrown on it, we cannot deny relationship between the two conditions.

316 Wall Building.

88. Compare similar reports. Roxburgh, A. C.: Brit. J. Dermat. **35**:152 (April) 1923. Gismondi, A.: Pediatria **30**:1114 (Dec. 1) 1922; abstr., J. A. M. A. **80**:284 (Jan. 27) 1923. McClean, J. F.: Lancet **1**:283 (Feb. 10) 1923. Von Barabas, Z.: Jahrb. f. Kinderh. **100**:331 (Jan.) 1923; abstr., J. A. M. A. **80**:1349 (May 5) 1923. Berinsohn, H. W.: Nederlandsch Tijdschr. v. Geneesk. **1**:2097 (May 10) 1924; abstr., J. A. M. A. **83**:162 (July 12) 1924. Von Bókay, J.: Jahrb. f. Kinderh. **105**:8 (March 5) 1924; abstr., J. A. M. A. **82**:1404 (April 26) 1924.

89. Condat: Arch. d. méd. d. enf. **26**:77 (Feb.) 1923.

90. Vaglio, R.: Pediatria **32**:650 (June 1) 1924.

Abstracts from Current Literature

Anatomy and Physiology

ON THE TYPE OF SUGAR EXCRETED IN URINE OF NORMAL PERSONS. KENNETH TALLERMAN, Biochem. J. **18**:583, 1924.

The sugar excreted in the urine of a normal subject as a result of an injection of phlorizin, is not γ glucose but appears to be the ordinary α-β variety. Since there is no evidence for the presence of γ-glucose in the urine of a healthy person, the sugar passed by the diabetic patient is of the same nature as that of the normal person.

THE RELATIVE INFLUENCE OF MENTAL AND MUSCULAR WORK ON THE PULSE RATE AND BLOOD PRESSURE. R. D. GILLESPIE, J. Physiol. **58**:425, 1924.

Mental work produces an increase in pulse rate and blood pressure. The increase is independent of emotional factors. The increase is not accounted for by movements of articulatory muscles. In combined mental and muscular work, the increase in pulse rate and blood pressure are greater than in mental or muscular work performed singly.

KUGELMASS, New Haven.

BREAST MILK LIPASE. WERNER GOTTSTEIN, Jahrb. f. Kinderh. **106**:97, 1924.

Lipolytic milk ferment was found in colostrum, in milk at any time of the day, at the beginning and at the end of the lactation period. This ferment is destroyed by heating but not by standing at room temperature, and may be more active after mechanical shaking, for example in the infant's stomach. This lipase is not present in cow's milk.

In dyspepsias there is a disturbance of fat digestion, which is made worse by the addition of any kind of fat except breast milk fat. The explanation is offered that there is a destruction of stomach lipase in dyspepsias, so that fat digestion must then be started by breast milk lipase, and if breast milk is not available fat digestion is incomplete.

In the infant's stomach after breast milk coagulation, the conditions are favorable for the activity of either breast milk lipase or gastric lipase. The breast milk whey is more favorable for the fat splitting action of gastric lipase than in cow's milk whey, while the milk lipase is more active when gastric juice is added, even though the gastric lipase has been destroyed.

PROTEIN DIGESTION IN THE INFANT. E. FREUDENBERG and E. A. STERN, Jahrb. f. Kinderh. **106**:109, 1924.

Tryptic digestion by the duodenal juice of infants was no more rapid whether breast or cow's milk was used. This relation was not changed by previous coagulation. The idea of difficult digestion of protein from a different species is not supported.

DETERMINATION OF ACTUAL STOMACH ACIDITY IN THE BREAST FED INFANT. H. BEHRENDT, Jahrb. f. Kinderh. **106**:115, 1924.

When the breast milk lipase was inactivated by heating, the acidity of the gastric contents one and one-half hours after feeding was less than when the milk was not heated. Thus the H-ion concentration of the stomach contents is definitely increased by the lipolysis of fats to fatty acids. Breast milk in

which the lipase had been activated by heating at 35 to 40 in vacuo after coagulation by rennin, contained considerably more fatty acid than that in which the coagulation had not been carried out previously. The milk lipase is therefore activated by rennin coagulation.

SUTHERLAND, Chicago.

Pathology, Bacteriology and Biochemistry

YEAST GROWTH-PROMOTING VITAMIN TESTED FOR ITS EFFECTS ON ANIMALS. J. DEAS, J. Biol. Chem. **61**:5, 1924.

Experiments were made on animals using Bios I and Bios II and the malt rootlets from which they were obtained. Bios I and II are vitamins necessary for the growth of yeast. However in rats, on a vitamin-free diet, these products were inefficient in producing growth. They also had no antiscorbutic property.

STUDIES OF THE EFFECT OF EXERCISE IN DIABETES. II. LACTIC ACID FORMATION IN PHLORHIZIN DIABETES. ROBERT O. LOEBEL, DAVID P. BARR, EDWARD TOLSTOI and HAROLD E. HIMWICH, J. Biol. Chem. **61**:9, 1924.

Dogs were given phlorizin and rendered diabetic. Some of these animals were also given epinephrin to render them as glycogen-free as possible. When these animals were thrown into strychnin convulsions, lactic acid was formed, even when no carbohydrate was being burned. The authors believe that lactic acid is formed from carbohydrate in these cases, but that the carbohydrate is formed again from the lactic acid by energy from the combustion of fat.

IS THERE A TOXIN IN THE BLOOD OF PARATHYROIDECTOMIZED DOGS? ISIDOR GREENWALD, J. Biol. Chem. **61**:33, 1924.

An extract was made from the blood of parathyroidectomized dogs in active tetany. This extract was injected into parathyroidectomized dogs which did not have tetany. These injections did not cause convulsions as occur in tetany. Therefore the author does not believe parathyroid tetany is due to a toxin which is normally neutralized in that gland.

A NOTE ON THE RÔLE OF THE LIVER IN PARATHYROID TETANY. JULIUS BLUMENSTOCK and ALBERT ICKSTADT, J. Biol. Chem. **61**:91, 1924.

This is a preliminary paper in which the authors report the effects of parathyroidectomy in dogs with an Eck fistula. The symptoms of tetany were delayed, but remained persistent after they appeared unless the animal received calcium. The authors suggest that the liver modifies intestinal toxins to cause tetany.

A STUDY OF THE EFFECT OF TEMPERATURE ON PROTEIN INTAKE. W. DENIS and P. BORGSTROM, J. Biol. Chem. **61**:109, 1924.

Medical students in New England showed almost double the nitrogen metabolism of those in Louisiana. The students in the colder months (February and March) showed higher nitrogen metabolism than in April and July. The authors conclude that there is a tendency for people to eat less protein in the warmer parts of the country and during the warmer seasons of the year.

HIGGINS, Cincinnati.

A UNIFORM METHOD FOR THE ESTIMATION OF GLUCOSE IN BLOOD AND URINE. HOWARD D. HASKINS, AND W. PAUL HOLBROOK, Northwest Med. **23**:355 (August) 1924.

For the details of this method the reader is referred to the original article. The authors describe the technic to be followed in estimating the glucose of

the blood and urine by the same method. This method is a modification of the Shaffer and Hartmann iodometric titration method. It eliminates special reagents and special technic for urinary sugar and has the advantage that simultaneous blood and urine determinations can be run rapidly. They furnish a special table which gives a direct reading of glucose percentage to correspond with the amount of titrating agent used.

POST-TRANSFUSION REACTIONS. HARRY H. KRETZLER, Northwest Med. **23**:358 (August) 1924.

About 49 per cent. of the transfusions were given in cases of pernicious anemia and about 38 per cent. in cases of secondary anemia. Sixty-four cases were done by the citrate method and thirty-seven by the syringe method. The citrated patients showed eight times as many chills, ten times as many instances of nausea and vomiting, and showed much more pronounced temperature and pulse rises.

ARTIFICIAL ENLARGED THYMUS; SUPPLEMENTARY REPORT. L. HOWARD SMITH, Northwest Med. **23**:368 (August) 1924.

Smith injected from 0.5 to 3.5 c.c. of melted paraffin into the thymus region of guinea-pigs. These were carried by the pigs without symptoms and at necropsy the artificially enlarged thymus was found. By adding 10 per cent. of barium sulphate to the paraffin, a roentgenogram could be obtained. These were shown in the text of the article.

SCOTT, Philadelphia.

THE ANTISCORBUTIC VALUE OF FRESH AND CANNED ENGLISH TOMATOES. ELLEN MARION DELF, Biochem. J. **18**:674, 1924.

The minimal daily ration of raw fresh juice of English tomatoes protecting young guinea-pigs from scurvy is between 1.5 and 2.5 c.c. and hence not as effective as fresh orange or lemon juice. Canned tomatoes lost three-fourths and canned tomato puree lost seven-eighths of the original value.

THE ANTISCORBUTIC FRACTION OF LEMON JUICE. SYLVESTER SOLOMON ZILVA, Biochem. J. **18**:632, 1924.

The active antiscorbutic fraction of lemon juice contains only from 0.03 to 0.07 per cent. of solid matter in solution. It reduces ammoniacal silver nitrate and decolorizes potassium permanganate; it is low in nitrogen and phosphorus.

CHOLIN IN THE BLOOD AFTER PARATHYROIDECTOMY. W. F. SHANKS, J. Physiol. **58**:466, 1924.

After parathyroidectomy the serum, in cases where the symptoms are well developed, contains a larger amount of cholin than normal serum does from the same animal before operation.

KUGELMASS, New Haven.

STUDIES ON RESPIRATORY DISEASES. XVIII. THE RELATIVE RELIABILITY OF THROAT SWABS FOR ISOLATING THE CAUSATIVE PNEUMOCOCCUS TYPE. FRANK B. KELLY and HARRY GUSSIN, J. Infect. Dis. **35**:323, 1924.

Observations were made in 136 cases of lobar pneumonia to determine the reliability of throat swabs as compared with raised sputum and blood culture from the same patient, as a means for isolating the causative pneumococcus type. The technic for the preparation and examination of the smears, sputums and blood are given in the article.

It was found that the ratio of positive throat swabs to positive sputums and to positive blood cultures was equal to 1 or nearly 1.

The conclusions reached were that throat swabs are relatively easy to make and prevent discomfort to the patient, that they are reliable for the determination of the type of the causative pneumococcus organism, and that they are of especial value in obtaining pneumococci from children with lobar pneumonia. Contamination with saliva from the mouth seemed not to interfere in the determination of the causative type of pneumococcus.

STUDIES ON RESPIRATORY DISEASES. XIX. UNTREATED BILE AS A SOLVENT FOR PNEUMOCOCCI. FRANK B. KELLY and HARRY GUSSIN, J. Infect. Dis. **35**:327, 1924.

Tests were made on the solubility of pneumococci in 10 per cent. sodium taurocholate, autoclaved whole bile and untreated whole bile which had been kept on ice for two and one-half months. Twenty-four hour glucose broth cultures of forty-one strains of pneumococci, including ten strains of Type 1, eight of Type 2, five of Type 3, and eighteen of Type 4 were used. It was found that stored, untreated, whole ox bile dissolves pneumococci better than the bile preparations ordinarily used. It dissolves dextrose broth cultures readily with no interference from precipitation. Misinterpretation of Nicolle and Adil Bey's reports has been a factor in the failure to recognize these points.

KENNEDY, Rochester, Minn.

CARBONATE TENSION OF THE BLOOD AND CEREBROSPINAL FLUID IN DIFFERENT DISEASES OF CHILDHOOD. ZOLTÁN VON BÓKAY, Jahrb. f. Kinderh. **106**:120, 1924.

Rohony's method was used, though normal values were from 130 to 170 instead of the range 125 to 160 given by Rohony. Five hundred and eighteen samples from 338 children were examined. The blood of infants under 1 month of age gave low values, one as low as 70, but the value increased after 4 weeks of age to within normal limits. There was usually a decrease during the acute infectious diseases, in the exanthemas, especially at the beginning of the rash. The author did not find cases of outspoken alkalosis. Rickets, and especially spasmophilia, gave lower figures, one being 47. In cases of diabetes with acidosis, the carbonate tensions ranged from 19.5 to 66.

In general, the carbonate determinations on spinal fluid paralleled the results on blood plasma, though cases were frequently found in which the carbonate was higher than the normal range.

THE TRYPANOCIDAL CONTENT OF CHILDREN'S SERUM. PART 2. RESEARCHES ON KERATOMALACIA AND EDEMATOUS CONDITIONS. S. GRÜNMANDEL and B. LEICHTENTRITT, Jahrb. f. Kinderh. **106**:203, 1924.

The trypanocidal content of the blood is taken as an index of the child's resistance. In keratomalacia, this resistance is uniformly very low. This accounts for the frequency of infections complicating avitaminosis. In edematous conditions as cachectic edema, nephritis and cardiac edema, there is a decrease in the trypanocidal substance.

THE TRYPANOCIDAL CONTENT OF CHILDREN'S SERUM. PART 3. RESEARCHES ON CHILDHOOD SCURVY AND RELATED CONDITIONS. S. GRÜNMANDEL and B. LEICHTENTRITT, Jahrb. f. Kinderh. **106**:215, 1924.

The changes in the blood vessel walls, and the resulting bleeding are only a part of the general tissue injury. The authors consider the loss of protective power of the serum to be due to an injury of the reticulo-endothelial system.

SUTHERLAND, Chicago.

Nutrition

HYPOGLYCEMIA AND ACIDOSIS. FRITZ B. TALBOT, EDWARD B. SHAW and MARGARET E. MORIARTY, J. A. M. A. **83**:91, 1924.

In eight fasts carried on in five children as treatment of idiopathic epilepsy, a ketosis was found. The ketosis was accompanied by a low blood sugar concentration. It is thought that the acidosis during voluntary fasting and involuntary starvation is due to a diminished amount of available sugar in the body. Clinically when a ketosis is found, it may be assumed that there is some interference with the availability of the sugar or with the ability of the body to oxidize sugar. The low sugar concentrations found during fasting give the underlying reason for the efficiency of glucose in the treatment of acidosis. The administration of carbohydrate is seen to complete the combustion of the ketone bodies. With the hypoglycemia there is suggested the possibility of danger in use of insulin in cases of acidosis during fasting.

THE FOOD REQUIREMENTS OF MALNOURISHED INFANTS, WITH A NOTE ON THE USE OF INSULIN. W. MCKIM MARRIOTT, J. A. M. A. **83**:600, 1924.

Marriott believes that in the case of an undernourished infant, if he weighs only half of what he should for his age, the total food requirement is likely to be in the neighborhood of 100 calories per pound. A malnourished baby may gain on less, but satisfactory results are not often obtained unless the amounts of food indicated are given. Some infants fail to gain even when the nutritional requirements have been met, and to these infants are usually given repeated transfusions of matched citrated blood. The amount given is usually about 20 c.c. blood per kilogram of body weight.

Besides oral methods the intravenous methods may be used. Glucose can be given intravenously in a 20 per cent. solution, provided the injection is given slowly. The amount of the injection should be from 20 to 30 c.c. per kilogram. Glucose given in this way is only partly utilized, but if insulin is given at the same time, better utilization of the sugar occurs.

Six cases are reported that bear out the statement made by Marriott.

HENN, Chicago.

A CLINICAL STUDY OF LACTIC ACID MILK AS A ROUTINE FEEDING FOR SICK AND HEALTHY INFANTS. M. C. FIELD, Arch. Pediat. **41**:541, 1924.

An analysis of seven infants fed on lactic acid milk with karo corn syrup added is presented. All the babies were healthy and thriving well on the food. The total number of days they had received the milk exclusively was 282, the net gain 359 ounces or an average daily gain of 1.3 ounces. The babies were firm, happy, vigorous, of good color, slept well and had no colic. Difficulty was often encountered in feeding the milk to older infants and children, some refusing it altogether.

EXPERIENCES WITH LACTIC ACID MILK IN INFANT FEEDING. M. GLEICH, Arch. Pediat. **41**:548, 1924.

The author concludes that lactic acid milk is no panacea although it has a valuable place in the armamentarium of the pediatrician. Considering athreptics as difficult feeders, lactic acid milk is an excellent means of helping them. It gives them concentrated food and by virtue of its acidity enables them to digest it more readily than sweet milk. Furthermore, by increasing gastric acidity it may play an important rôle in the prevention of rickets and tetany.

VON MEYSENBUG, New Orleans.

THE EFFECT OF COD LIVER OIL IN VARIOUS AMOUNTS AND FORMS ON THE GROWTH OF YOUNG CHICKENS. L. C. DUNN, J. Biol. Chem. **61**:129, 1924.

Groups of approximately twelve chickens each were given a diet containing no antirachitic or fat-soluble vitamin and were kept in confinement. Cod liver oil was added to these diets in quantities equivalent to 0.25 per cent., 0.50 per cent., 1 per cent. and 2 per cent of the total feeding. The birds getting 0.25 per cent. cod liver oil developed rickets. The chickens getting 0.50 per cent. or more cod liver oil grew normally, those receiving 0.5 per cent. growing as well as those receiving more. Cod liver oil loses some of its vitamin quality on storage in a granulated starch mixture.

THE EFFECT OF HEAT TREATMENT OF MILK FEEDINGS ON THE MINERAL METABOLISM OF INFANTS. AMY L. DANIELS and GENEVIEVE STEARNS, J. Biol. Chem. **61**:225, 1924.

Metabolism experiments on artificially fed babies were made, comparing the calcium, phosphate and nitrogen retention when babies were fed (1) Pasteurized milk (slow heating), and (2) boiled milk (quick heating). There was a greater retention of these materials in the latter feeding. The curves of the calcium phosphate and nitrogen retention tended to be parallel.

CHANGES IN THE SERUM PROTEIN STRUCTURE OF RACHITIC RATS WHILE FED WITH COD LIVER OIL. STEPHEN A. P. EDERER, J. Biol. Chem. **60**:621, 1924.

Rachitic rats, on being treated with cod liver oil, show a diminished proportion of albumin and an increased proportion of globulin in the blood serum.

THE EFFECT OF ACUTE SCURVY ON THE SUBSEQUENT NUTRITION AND GROWTH OF GUINEA-PIGS. WILLIAM E. ANDERSON and ARTHUR H. SMITH, J. Biol. Chem. **61**:181, 1924.

Several pairs of growing guinea-pigs were studied. One of each pair received a basal diet plus raw cabbage and the other the same diet except that the cabbage was cooked and dried. The latter animals developed scurvy in approximately forty-five days. They were then put on the same diet as the control animals and their weight increased at the same rate or faster than the weight of the control animals. Scurvy does not affect later growth or nutrition.

HIGGINS, Cincinnati.

DIET AND TISSUE GROWTH. II. THE REGENERATION OF LIVER TISSUE DURING NUTRITION ON INADEQUATE DIETS AND FASTING. ARTHUR H. SMITH and THEODORE S. MOISE, J. Exper. Med. **40**:209, 1924.

One group of white rats was placed on an otherwise adequate diet containing gliadin as the only source of protein, a second group on a diet containing gelatin as the protein, and in a third group food was withheld. The fasting rats and those on the gelatin diet lost weight, the rats on the gliadin diet remained practically stationary in weight. After subcutaneous administration of chloroform dissolved in sterile mineral oil, rats from each group were killed at intervals of twenty-four hours up to 168 hours and the livers studied histologically.

The relative toxicity of the chloroform in these inadequate dietary conditions is as follows: gelatin diet > fasting > gliadin diet.

The rate of regeneration of the liver cells in rats fed a diet in which gliadin is the only protein is about equal to that in animals on a diet containing casein as the source of nitrogen. On a diet containing its nitrogen as gelatin, and during fasting the regeneration is slower than on the gliadin diet.

The results indicate that the requirements for the essential amino-acids for growth of individual organs is less than that for correlated growth of the whole body.

McCLURE, Evanston, Ill.

THE INFLUENCE OF DIET AND SUNLIGHT UPON THE GROWTH-PRODUCING AND ANTIRACHITIC PROPERTIES OF THE MILK AFFORDED BY A COW. ETHEL MARJORIE LUCE, Biochem. J. **18**:716, 1924.

Milk from the same cow varies within wide limits in its antirachitic and growth promoting power. The diet of the cow is the main factor in determining the growth promoting value of the milk. When the cow received a diet of fresh green grass, the milk possessed a higher growth promoting value than when she received dry fodder deficient in fat-soluble vitamin. This result was obtained in sunlight as well as in darkness. The antirachitic value depends on the diet of the cow and possibly on the degree of illumination to which she is exposed. Milk from a pasture-fed cow has a definite and high antirachitic value; the same animal when stall fed in the dark yielded a milk much inferior in antirachitic properties. A possible contributory cause of the seasonal incidence of rickets in children may be the use of milk the antirachitic value of which is higher in summer than in winter.

KUGELMASS, New Haven.

CONSTITUTION AND NUTRITION. B. P. B. PLANTENGA, Jahrb. f. Kinderh. **106**:130, 1924.

This is a discussion of what is meant by constitution. It includes not only inherited characteristics, but also characteristics which are determined by environmental conditions. In considering the diatheses, he presents the idea of constitutional harmony and disharmony. In the latter group the disharmony may be toward different food substances, e. g., eczema may be due to disharmony toward fat, protein, carbohydrate, salts and individual foods such as eggs, cocoa and fruit. This disharmony may be manifested either on breast or artificial feeding. In the former case, the mothers diet must be corrected. After infancy, the disharmony may be manifested by other phenomena than those of infancy, e. g., urticaria, migraine, asthma, hay-fever, hyperacidity, diabetes, etc. Illustrative cases are given.

THE PATHOGENESIS OF ACUTE ALIMENTARY NUTRITIONAL DISTURBANCES. PART 13. THE KIND AND QUANTITY OF FERMENTATION ACIDS IN THE FERMENTATION OF SKIMMED MILK BY ENTEROCOCCI AND B. COLI. WERNER CATEL, Jahrb. f. Kinderh. **106**:145, 1924.

The author considers the acute nutritional disturbances to be due to substances which stimulate peristalsis to an abnormal degree, principally the short chain fatty acids such as acetic and butyric. Cultures of enterococci (*Streptococcus lacticus)* and *B. coli* were added to sterilized skimmed milk, and incubated for twenty-four to thirty hours. The *B. coli* milk after that period tasted stale and unpleasant; the enterococcus milk tasted like buttermilk. The acidity of the milk in the case of the *B. coli* was due mostly to short chain fatty acids, and in the other series to lactic acid. The enterococci are therefore relatively harmless, while *B. coli* may cause nutritional disturbances. Dyspepsia results when the concentration of lower fatty acids in the upper intestine is great enough to stimulate hyperperistalsis.

THE CLINICAL VALUE OF FAT DETERMINATION OF BREAST MILK. HANS KOEPPE, Jahrb. f. Kinderh. **106**:177, 1924.

Several cases are cited of breast fed infants whose intake would ordinarily be considered sufficient, but who were not gaining. The breasts were not being emptied, so that the milk with a high fat content was not being obtained. The

caloric intake was therefore insufficient. By partly emptying the breast just before the infant nursed, the fat intake was increased and a satisfactory gain in weight followed. Several other cases are cited in which the quantity of milk seemed insufficient by the usual method of calculation, but the milk had a fat content of from 7 to 12 per cent., so that the caloric intake was actually too high.

The fat was determined by the thickness of the cream layer after allowing the milk to stand, and then the energy quotient computed. This simple method adds a considerable degree of accuracy to the computing of breast feedings.

FERMENT STUDIES IN NUTRITIONAL DISTURBANCES OF CHILDHOOD. KANZAHURO HIZUME, Jahrb. f. Kinderh. **106**:227, 1924.

This is a study of the digestive enzymes present in the blood and excreta. 1. Lipase was present in the blood serum of dystrophic infants and cases of alimentary toxicosis in amounts only slightly less than in normal infants. In rickets, the amount was often greater than normal. 2. In the urine, lipase was occasionally present in much larger amounts than in adults. In dystrophies the amount varied within normal limits but was a little low. 3. Lipase in the feces was not present in greater amounts in normal than in dystrophic infants. In rickets the amount was somewhat greater than normal. 4. Diastase in the serum, stools, and urine was present in normal amounts in dystrophic infants. In rickets the values tend to be high. 5. In the urine of normal infants rennin, as prorennin, is found in small amounts, also small amounts of pepsin and erepsin. In a nephritic patient pepsin and erepsin in the urine were very much increased.

SUTHERLAND, Chicago.

DEFICIENCY OF THE HALOGENS IN MODERN DIETETICS. C. EDGERTON CARTER, M. J. & Rec. **120**:226, 1924.

In this article, the author discusses the question of the thyroid's ability to function effectively, as controlled by sufficient halogen intake. Many underlying conditions in simple goiter, cretinoid types, nervous and neurotic manifestations, rachitis and beginning epilepsy suggest a diet deficiency.

Suboxidation, with the consequent disturbance of normal cell activity through imbalance of required minerals and salts appear to be present in all conditions outlined above.

Many symptoms exhibited in children, such as malnutrition, retarded or imperfect dentition, rachitis, asthma, bronchitis and eczema, or revealed in dry skin, cold extremities or multiple adenitis, may be manifestations of subthyroidism which we are accustomed to so group only if definitely showing retarded mentality or marked degenerative stigmas.

To consider for a moment the practicability of attempting to assure a well nourished thyroid by means of supplying additional halogens as an aid to general oxidation and cell activity, Janney has emphasized that "the chief function of the thyroid is the generation and regeneration of the tissues by action of the thyroxin on protein metabolites."

Experiments and research work of three authoritative sources outside of the author's observation gives added impetus to certain angles in "the hypothesis of a dietetic deficiency."

KINBERGER, New Orleans.

CONCEPTIONS REGARDING THE PATHOGENESIS OF RICKETS. AUGUSTIN ZORRILLA Y POLANCO, Arch. Españ. Pediat. **8**:259, 1924.

The author discusses the etiology and pathogenesis of rickets under the head of theories, and groups these as follows: (1) the chemical, (2) the toxic, (3) the infectious, (4) the myelogenous, (5) the nervous, (6) the endocrine gland, (7) the heliopathic and (8) avitaminosis theory.

In discussing these various theories in detail, the author comes to the conclusion that in the development of rickets in an organism there exists: (1) a primary cause, either isolated or combined. Such a cause could be an intoxication, essentially of digestive origin, or an infection such as hereditary syphilis, or it may be deficiency of certain natural agencies, or a deficiency of vitamin factors; (2) There exists probably a secondary predisposing cause. This expresses itself as a constitutional debility and notably as a disfunction and abnormal alteration of the hormonopoietic system. This presumes a further secondary determining cause which expresses itself in disfunction, particularly hypofunction of certain endocrine structures.

The thymus, thyroid and parathyroids and suprarenals are the glands chiefly involved. The disfunction in these glands leads to alteration in the internal metabolism with loss of the equilibrium between the elements calcium and phosphorus. This loss of equilibrium leads to the immediate development of the rachitic dystrophy.

THE DIGESTIBILITY OF FRESH AND ACID COW'S MILK. D. ORLA-JENSEN, and BERNHARD SPUR, Ugesk. f. Laeger **36**:655, 1924.

The experiments showed that milk containing 0.5 per cent. lactic acid as in buttermilk was more slowly digested than the 1 per cent. lactic acid milk. The best digestion was observed in milk containing 1.5 per cent. lactic acid and 0.3 per cent. hydrochloric acid, approximating gastric acidity.

The extent of digestion was found by determining what percentage the nitrogen content of a filtrate from the digestion mixture was of the total nitrogen. Pepsin was used as the hydrolytic enzyme.

SCHLUTZ, Minneapolis.

Diseases of the New-Born

FAMILIAL STUDY OF THREE UNUSUAL CASES OF CONGENITAL ICHTHYOSIFORM ERYTHRODERMA. UDO J. WILE, Arch. Dermat. & Syph. **10**:487, 1924.

Wile reports three cases of unusual postnatal exfoliation. The first diagnosis was exfoliative dermatitis of the new-born, later this was changed to epidermolysis bullosa, because of the similarity of the histologic picture to the latter disease. More recently, the diagnosis was changed to congenital ichthyosiform erythroderma, based on the clinical and histologic findings. The unusual features of the disease were the irregularly distributed areas of superficial exfoliation associated with slight erythroderma, remarkably similar in all three children. All the children were undersized and marasmic. One of the children died at the age of 11 weeks, the oldest is now aged 4 years. Histologically, these cases are characterized by acanthosis, fragmentation and disorganization of the elastic tissue of the upper layers of the corium. The other remarkable feature was the occurrence of the disease in three male children, whose fathers were brothers and whose mothers were sisters, and whose grandparents were cousins twice removed. This brings up the question as to the possibility of consanguineous marriage as a probable predisposing factor of a recessive type of inherited dystrophy, also indicates an example of sex limitation in recessive inheritance. The histologic similiarity of the cases to the fundamental changes of epidermolysis bullosa of the dystrophic type, together with the fact that both diseases are recessive in their inheritance, suggests a close relationship between the two.

DERMATITIS EXFOLIATIVA NEONATORUM. J. EDGAR FISHER and S. S. WITTENBERG, Arch. Dermat. & Syph. **10**:289, 1924.

In the case reported by the authors, the first symptoms appeared on the sixth day after the birth of the child. Labor had been normal, and the child

was apparently well until the sixth day. The first lesions noted were flaccid bullae on the hands. Later bullae appeared on the face, trunk and feet, and by the third day the infant presented a typical picture of exfoliative dermatitis. No constitutional symptoms were noted other than a rise in temperature to 102 F. Examination of the serum from several bullae (taken under aseptic precautions), revealed a short chain streptococcus. The mother made an uneventful recovery, and at no time showed any skin lesions.

PEARSALL, Salt Lake City.

NATURAL IMMUNITY IN THE NEW-BORN. L. K. MUSSELMAN, Am. J. Obstet. & Gynec. **8**:141, 1924.

The author resumes his discussion of natural immunity in the new-born and considers the various methods by which the normally low potency of the serums may attain the adult value.

The placental transmission of preformed antibodies from mother to fetus plays a very small rôle, otherwise they would be nearer equal.

Cholestrin and milk do not contain normal antibodies measured by bactericidal test. They do, however, afford the tissues a better state of nutrition than artificial foods, thus enabling the tissues to develop a higher degree of resistance.

ALLEN, Chicago.

THYMUS OF NEW-BORN AND ITS SIGNIFICANCE TO THE OBSTETRICIAN. REUBEN PETERSON and NORMAN F. MILLER, J. A. M. A. **83**:234, 1924.

Observations were made on the incidence of thymic hyperplasia, and its significance in 120 infants consecutively born in the maternity division of the University Hospital.

It was found that with the older mothers the incidence of thymic hyperplasia increased. Babies of multiparas apparently are more apt to have an enlarged thymus than are those born of primiparas. Of the series studied, enlarged thymus occurred in 11 per cent. more males than in females. In general it was found that enlarged thymus is found in from 40 to 50 per cent. of the new-born. Symptoms indicative of thymic hyperplasia are generally absent the first day. There was found no appreciable weight or size difference between infants showing thymic hyperplasia and those with a negative thymus.

The roentgen ray is superior to clinical methods in arriving at an estimation of the size of the thymus.

HENN, Chicago.

BONE CHANGES IN CHONDRODYSTROPHY AND CERTAIN PECULIARITIES OF THE BONES OF THE NEW-BORN. D. D. LEBEDEW, Acta Pediat. **3**:290 (June) 1924.

In this pathologic study of eight cases, the author finds in varying degree the changes usually described in the cartilage: irregularity in shape, size and distribution of cells in resting cartilage; disordered arrangement of the proliferating cartilage without cell division or columnar arrangement; early calcification of the irregular cartilage; irregular erosion of the cartilage by the marrow vessels, producing isolated islands of cartilage and an uneven line of ossification. Besides these well recognized changes, he describes a metaplasia of cartilage into connective tissue near the perichondrium. At times the transition between these two tissues is so gradual that no sharp border can be made out.

Changes in the bone itself are described as a constant finding not observed previously and accelerated periosteal ossification takes place. This bone is irregular in structure and the bone cells show evidences of degeneration: nuclear changes such as pyknosis, karylysis, polymorphic nuclei, and amitotic

division. Empty Haversian canals are not infrequent. These changes are found not only in the long bones, but at times are equally striking in the bones formed exclusively from connective tissue, such as the clavicle and bones of the skull.

The evidences of disease vary greatly in intensity, not only in different cases, but in different bones and even in different parts of the same bone. The changes in the bone and cartilage, however, always run parallel.

Concerning the etiology of the disease, the author concludes that two factors play a part: (1) familial degeneracy and (2) an intoxication of some sort. Similar histologic pictures in the bones have been produced by silver nitrate and other poisons, although the lesions in the cartilages have not been duplicated. The evidence for degeneration lies in the familial character of the disease and the frequent association with other malformations.

In connection with some control studies on normal infants, the author describes a peculiarity of ossification in the long bones of the new-born. A small triangular area of somewhat abnormal bone is formed from connective tissue beneath the periosteoperichondral junction. This is later converted into normal bone. Its production is perhaps analogous to the preliminary calcification of cartilage.

HOLT, Baltimore.

CONGENITAL STENOSIS OF THE SMALL INTESTINE IN AN INFANT. C. HUETER, Jahrb. f. Kinderh. **106**:245, 1924.

Uncontrollable vomiting began in an infant, aged 4 days, but with some passage of fecal material. The child died, and on necropsy a narrow, partially constricting band was found, from 0.1 to 0.2 cm. wide, through which the muscular layers of the intestine did not extend. In the absence of active peristalsis across this point, the intestinal content could not be passed sufficiently, so that death from obstruction resulted. The lesion was thought to be the point at which the omphalomesenteric duct had arisen.

SUTHERLAND, Chicago.

Acute Infections

SCARLATINAL ARTHRITIS. ALEXANDER JOE, Edinburgh M. J. **31**:344 (June) 1924.

At the Edinburgh city hospital for contagious diseases forty-nine cases of arthritis were seen by the author, and 24,012 records of scarlet fever were used for statistics. No infant during the first two years of life had arthritis. Most arthritis appeared on the sixth and seventh days. Adenitis was the only complication related definitely with arthritis. In sixty-one cases of endocarditis and pericarditis twenty-six accompanied arthritis. The percentage incidence of arthritis in scarlet fever is 3.76. Arthritis is transient, affects one or more joints, has a febrile reaction, myositis may develop, but suppuration is rare. Only seven arthritic patients had a "dirty" throat, but thirty gave a history of definite previous rheumatism. In some cases a stiffness only appears, pain results in a peculiar helplessness in the wrist or finger joints. Pain but not tenderness may be the only symptom. Thirty of forty-nine cases watched for swelling were negative, swelling when present was mild chiefly in the wrist and fingers; enlargement not due to much fluid involves the periarticular tissues, is transitory and never accompanied by redness. Pain and pyrexia give the first warning, the peak's recurring as new joints are involved. Age played no part in the joint distribution which is often symmetrical; an average of four joints in males and five in females. Myositis in 22 per cent. of the forty-nine cases involved the arm, forearm, quadriceps, calf, lumbars, trapezius and sternomastoid in the order named. In 700 cases of septic scarlet fever, arthritis accompanied it in only about 5 per cent. of males, but in 15 per cent. of females.

NEFF, Kansas City.

AMIDOPYRIN IN THE TREATMENT OF MEASLES. MAX LOWENTHAL, Brit. M. J. **2**:51, 1924.

The author recommends this drug as a specific for measles just as quinin in malaria. The results observed, if given at the first appearance of the rash are:

1. Reduction of temperature to normal or nearly normal within twelve hours.
2. Inhibition of the rash.
3. Immediate euphoria with relief of the distressing symptoms associated with measles.
4. Prompt relief of the catarrhal symptoms.

The dose recommended for the adult is 12 grains (0.780 gm.) three times a day and for the child the following formula $\frac{\text{Age} \times 1 + \text{dose}}{24}$

No untoward effects have been observed.

BROWN, Toronto.

EXPERIENCE GAINED FROM AN EPIDEMIC OF PERTUSSIS FROM AUGUST 1923 UNTIL SUMMER 1924 IN OR NEAR THORSHAVN. HJ. HEERUP, Ugesk. f. Laeger **37**:675, 1924.

The clinical findings show that the giving of pertussis vaccine has no effect on the course of the disease after it has fully developed.

In a series of vaccinated children, it was observed that the stronger the local reaction the more mild was the course of the disease. No deaths occurred among the vaccinated children, but did occur among those not vaccinated.

INVESTIGATIONS INTO SHICK'S REACTION IN CHILDREN. POVL HERTZ, Ugesk. f. Laeger **33**:612, 1924.

Shick's reaction was observed in two groups of children, the one group from 1 to 6 and the other from 6 to 16 years old. In the first group, the reaction was positive in 80 per cent.; in the second group in 43 per cent. of the children.

The pseudoreaction, which frequently occurs, was investigated. The author considers that the pseudoreaction is due to endotoxins of bacteria. To determine the presence of this endotoxin, an intracutaneous injection of the boiled toxin-antitoxin is made into the right arm so as to act as a control for the toxin-antitoxin injection of the left arm.

It was observed that the psuedoreactions do not always disappear in forty-eight hours and that scaling and pigmentation may be present as in the toxin-antitoxin reaction. It therefore becomes important to immunize in the doubtful patients.

FREQUENCY, LOCALIZATION AND CLINICAL FORMS OF INFANTILE PNEUMONIA. A. ROMEO LOZANO, Arch. Españ. Pediat. **8**:193, 1924.

The author reports his findings and observations on ninety-four cases. The process involved the left lung in forty-six cases, the right in forty-seven cases, and both in one case.

The involvement of different lobes was as follows:

The left inferior lobe in thirty-one cases; the right superior lobe in twenty-three; the right inferior lobe in eighteen; the left superior in six; both left lobes in nine; two right lobes in five.

These figures do not confirm the observations of Engel that the right lung is more frequently affected than the left.

The author divides the clinical forms of infantile pneumonia into the following types:

1. The abortive form. Cadet de Gassicourt has described them under the term of simple idiopathic pulmonary congestions. About ten cases out of a hundred are of this type.

2. The prolonged type. This type comprises several phases. In the first phase a rhinopharyngitis or angina is mainly observed. In the second phase there is a bacteremia; and in the third phase there is the localization of the process in the lungs in the form of pneumonia. These types often pass under the title of typhoid pneumonia.

3. The migrating type, localized at the beginning in some portion of the lung and extending from there to adjoining portions and gradually involving the entire lung.

4. A type showing predominance of nervous phenomena and often nearly masked by these.

Rilliet and Barthez designated these types as the eclamptic and the meningeal type, the latter being accompanied by either delirium or coma. Convulsions characterize the eclamptic form.

The comatose form is characterized by excessive prostration and complete indifference to the environment.

The delirious type may take on the form of hallucinations or violent delirium.

Meningeal phenomena are present in all three forms.

ETIOLOGY AND PATHOGENESIS OF PYELITIS AND PYELONEPHRITIS IN NURSLINGS. D. JUAN GONZÁLEZ EDO, Pediat. Españ. **13**:78, 1924.

Pyelitis in nursing infants is a relatively frequent condition. Clinically it is commonly overlooked on account of the absence of subjective symptoms in the sick infant.

It is always secondary to other infections. They may act as a predisposing cause in various ways. They may affect only the lower urinary passages or may involve only the upper part of the urinary tract, especially the pelvis of the kidney.

The infective agent may be conveyed by either the lymphatic or the hematogenous route. The latter is doubtless the more common.

SCHLUTZ, Minneapolis.

A CASE OF RECURRING SCARLATINA. E. BOSCHI, Riv. di clin. Pediat. **22**:546, 1924.

Boschi has collected the cases of recurring scarlet fever reported since the year 1900, and added a report of one of his own.

This patient, while recovering from scarlatinal nephritis five months after the onset of the scarlet fever which gave rise to it, had a second typical attack of the fever. Boschi believes these "recidival" cases to be the result of the reassumption of pathogenic activity on the part of the causative organisms left in the body from the first attack and not of a new infection from without.

A BRIEF REPLY TO PROFESSOR AMATO CONCERNING THE ETIOLOGY OF SCARLET FEVER. G. CARONIA, Riv. di clin. Pediat. **22**:241, 1924.

A reply of the author's to certain strictures of Professor Amato, concerning the identity and specificity of the organism described by the author and Sindoni as the etiologic agent of scarletina.

VACCINE THERAPY IN PERTUSSIS. G. VITETTI, Riv. di clin. Pediat. **22**:386, 1924.

The author reports a series of 105 children treated with pertussis vaccine with the following results: cured, from 67 to 63.8 per cent., improved, from 31 to 29.52 per cent., unbenefited, from 7 to 6.6 per cent.

SHIPLEY, Baltimore.

EXUDATE, SPINAL FLUID AND BLOOD FINDINGS IN ACUTE JOINT RHEUMATISM IN CHILDHOOD. JOHANN VON PETHEÖ, Jahrb. f. Kinderh. **106**:141, 1924.

The author's object was to determine the nature of rheumatism in children. Not finding bacteria by microscopic examination of the fluids, or by cultures on

different mediums, he concludes that the joint condition is the result of toxemia and not a direct infection of the point. He also obtained a four plus Wassermann on the joint fluid as well as on the blood and spinal fluid in all cases, syphilitic and nonsyphilitic. In the nonsyphilitic patients, the degree of the reaction decreased as the acute symptoms subsided. The writer does not offer an explanation of these findings.

SUGGESTION THERAPY IN WHOOPING COUGH. ARTHUR ZANKER, Jahrb. f. Kinderh. **106**:195, 1924.

The author attempts to control the neurotic element in whooping cough by suggestion. First the child is given painful injections of ether (1.0) and camphor (0.5), or 5 per cent. silver nitrate or milk injections (3 c.c.) once or twice daily. These injections had no effect on the number of paroxysms. Then the injections were stopped for several days. Then a "threat injection" of the same material was given at the height of a paroxysm. Suggestion therapy was then started. The patient was urged not to cough and threatened with more injections if he did cough. This suggestion was frequently repeated on this and succeeding days by someone who was with the patient. The result was a marked decrease in the number of paroxysms from the time of the "threat injection." The paroxysms occurring during sleep at night continued for several days longer than paroxysms during the day, but even the paroxysms at night decreased promptly in number. Six cases are reported, treated according to this plan.

This method of treatment is effective only after about 3 years of age as the effect depends on the intelligence of the patient.

SUTHERLAND, Chicago.

Chronic Infections

AN ATTEMPT TO VACCINATE CHILDREN AGAINST TUBERCULOSIS. NATHAN RAW, Brit. M. J. **2**:102, 1924.

The writer has been carrying on further observations on his new tuberculosis immunizing vaccine (Brit. M. J., April 23, 1921), which he had prepared from dead cultures that had become attenuated through frequent subculturing over a period of fourteen years. Five series of experiments are described, after which he concludes that it is possible to immunize animals against tuberculosis by means of a protective vaccine prepared from these attenuated bacilli. The duration of the immunity is not known. As a result of these observations the work was carried further, and he vaccinated 412 children from the age of 1½ to 14 years, in whom one or other of the parents were suffering from tuberculosis. Two doses of dead cultures of attenuated bovine bacilli were given at an interval of two weeks, and no untoward reactions were observed. He was unable to draw any conclusions until more time for observation had elapsed.

BROWN, Toronto.

DISCUSSION ON CONGENITAL OR INHERITED SYPHILIS. Tr. Med.-Chirurg. Soc., Edinburgh, Edinburgh M. J. **31**:97 (Feb.) 1924.

David Lees opened the discussion of congenital syphilis with an extensive description of the transmission of the infection to the fetus, the diagnosis in the child, the regional involvements, the predisposition to intercurrent diseases, the prognosis which in the newborn is especially bad, and finally the treatment. Antenatal treatment has apparently been more widely practiced in Scotland than in America and is worthy of general practice. He prefers in the child the intramuscular injection of sulpharsphenamin in conjunction with the intramuscular injection of mercurial oil or mercury salicylate, the metallic mercury causing neither pain nor abscess formation. Inunction is next best if the mother will persist in it, though it sets up a stomatitis and gastro-enteritis more

frequently than intramuscular injection. He thinks intravenous injections are excreted too rapidly for constant effect, unless injected every second or third day. Mercury with chalk is the least efficacious. He regards the new treatment with metallic bismuth as the best adjuvant to arsenic. Prolonged treatment is a necessity.

In the discussion that followed, Dr. Leonard Findlay of Glasgow spoke at length of his experience wherein he found congenital syphilis less common than ordinarily thought, 3.4 per cent. of 1,034 sick hospital children having a positive Wassermann and something over 1 per cent. had apparent lesions. He spoke of the erratic behavior of syphilis in the different children of a family, some members healthy with no serum reactions or symptoms. He is disappointed as a rule, with the treatment of a syphilitic child, and recommends the treatment of the pregnant mother as the best method.

Prof. B. P. Watson said that a weak positive reaction in a pregnant mother may become negative subsequent to pregnancy and is therefore not diagnostic.

Dr. J. V. Patterson ascribes the fact of relative infrequency of congenital syphilis in private practice as due to parental treatment before marriage. Interstitial keratitis will run its course and subside without treatment, but there will be permanent loss of transparency in the cornea, and a scarring of the choroid and retina. Treatment was of great value in shortening the disease and reducing its disasters.

Dr. J. S. Fraser has not known any benefit from treatment in congenital syphilitic deafness.

Scott Shirving referred to the incomplete eradication of the spirochetes in congenital syphilis as a tragic result, in the light of modern advances in treatment.

Mr. Lees believes in continuing the treatment of the mother through pregnancy and puerperium and later until cured.

NEFF, Kansas City.

SPECIFIC ANTITUBERCULOSIS THERAPY IN PEDIATRICS. PIERO BRUSA, Riv. di clin. Pediat. **22**:505, 1924.

The author describes the results of the treatment of various manifestations of tuberculosis in 118 infants and children with Martinotti's antitubercular vaccine during a period of thirty-four years. Brusa finds this treatment beneficial in cases of tuberculous peribronchial adenitis but not in cases showing ulcerative pulmonary lesions.

No untoward results followed the administration of the vaccine according to instructions.

A STUDY OF THE TREATMENT OF THE CONGENITAL SYPHILIS WITH BISMUTH. GIAU CARLO BENTIVOGLIO, Riv. di clin. Pediat. **22**:478, 1924.

A study of sixteen cases of infants treated with potassium sodium bismuth tartrate, metallic bismuth and bismuth sodium citrate. Bentivoglio's cases seemed to show that treatment with these drugs has a favorable influence on syphilitic craniotabes, paronychia, coryza and on some nervous manifestations of syphilis. Splenomegaly and syphilitic osteochondritis were not benefited. He was able to get negative Wassermann reactions in blood and spinal fluid from treatment with bismuth. There was no severe local or general reaction following injection of the bismuth. Following the injections, the author observed a polymorphonuclear leukocytosis and a relative decrease in the mononuclear group, and a temporary depression of hemoglobin not to be confounded with the permanent depression of the latter which is the result of overdosage of bismuth. The preparations used are believed to be superior to metallic bismuth, especially potassium sodium bismuth tartrate. Mercury should be given in combination. Dosage must be regulated by the weight of the child and the hemoglobin percentage of the blood.

SHIPLEY, Baltimore.

AN INQUIRY INTO THE DEATH RATE DUE TO TUBERCULOSIS DURING THE FIRST FIVE YEARS OF LIFE. ADOLF LICHTENSTEIN, Acta Pediat. **3**:397 (June) 1924.

From statistics in the different counties of Sweden, Lichtenstein finds that the infant mortality from tuberculosis runs parallel to the general mortality from that disease. No connection can be traced between the incidence of tuberculosis in cattle and the infantile mortality from tuberculosis.

CONTRIBUTION TO THE HISTOPATHOLOGY OF THE SPINAL CORD IN CONGENITAL SYPHILIS. CORNELIA DE LANGE, Acta Pediat. **3**:385 (June) 1924.

The author reports histologic examinations of the spinal cords of two congenital syphilitic patients. Particular attention is called to retardation of myelinization and to the diminished number and size of the anterior horn ganglion cells. There changes have rarely been described in syphilis. The defective ganglion cells are thought to be aplasia rather than atrophy, a lack of development rather than a destruction of cells already formed.

SYPHILITIC MYOCARDITIS IN CONGENITAL SYPHILIS. NICOLAI JOHANNSEN, Acta Pediat. **3**:419 (June) 1924.

Two cases of congenital syphilis are reported in which interstitial myocarditis with round cell infiltration was found at necropsy. One of these children died very suddenly; the other developed symptoms of collapse a few hours before death which might possibly be interpreted as cardiac failure. From a study of the literature, Johannsen finds that cardiac involvement in congenital syphilis is much more common than is usually supposed. Interstitial changes are more frequent than gummas. Clinical symptoms are at times so striking as to lead to a diagnosis of congenital heart disease. Sudden death is not uncommon, and a bad prognosis should be given to any cases of syphilis showing symptoms of cardiac involvement.

HOLT, Baltimore.

A USEFUL AND INEXPENSIVE BISMUTH EMULSION FOR INTRAMUSCULAR TREATMENT OF SYPHILIS. SVEND LUMHOLT, Ugesk. f. Laeger **30**:569, 1924.

The author recommends in this article a useful and inexpensive bismuth emulsion for the intramuscular treatment of syphilis. He is quite impressed with the usefulness of this treatment.

The preparation he uses is bismuth hydroxid, $Bi(OH)_3$, in glycerin. The emulsion is prepared in the following manner. Ten grams of bismuth hydroxid are added to 5 c.c. of glycerin with sufficient distilled water added to make a mixture of 50 c.c.

On account of its content in metallic bismuth, this mixture rapidly becomes sterile. This mixture is not very stable and must be shaken well immediately before using.

The injections are somewhat more painful than similar oil emulsions of the preparation. The advantage of this preparation lies in the fact that the bismuth is absorbed much more rapidly in this form than in oil or paraffin emulsion. This results in a more rapid and direct effect, and the risk of the dangerous "depot-formation" is much less than with oil emulsions.

VIEWS ON THE MODERN THERAPY OF SYPHILIS. OTTO HASLUND, Ugesk. f. Laeger **36**:656, 1924.

The present tendency of gradually increasing the intensity of the treatment with the new antisyphilitic remedies is criticized.

In the author's estimation, the fact is not to be overlooked that the antisyphilitic preparations are injurious to the organs of the body. No doubt exists that the spirochete is killed by the drugs but at the expense of irritation of healthy tissue.

SCHLUTZ, Minneapolis.

Internal Diseases

THE RELATIONS BETWEEN A CARNIVOROUS DIET AND MAMMALIAN INFECTIONS WITH INTESTINAL PROTOZOA. ROBERT W. HEGNER, Am. J. Hygiene **4**:393 (July) 1924.

Observations and experimental data indicate that a carnivorous diet is unfavorable for entozoic protozoa that inhabit the intestinal tract.

Rats heavily infected with protozoa, when subjected to a carnivorous diet, show a slight falling off of the incidence of infection. At the same time the contents of the intestine changes from predominantly acidophilus type to a predominantly putrefactive type.

Examinations were made of fecal specimens at intervals during a period of seventeen days from twelve carnivorous animals belonging to ten species and no protozoa of any kind were found except giardia cysts in the wild cat, in one instance.

PRICE, Pittsburgh.

RECTAL DIGITALIS THERAPY. ROBERT L. LEVY, Arch. Int. Med. **33**:742, 1924.

The author states the present study was undertaken to ascertain the feasibility of rectal digitalis therapy. He cites a number of conditions coincident with myocardial insufficiency which precludes the administration of this drug by mouth, and adds that the rectal method is to be regarded as an emergency measure to be used particularly in the presence of nausea and vomiting, or after surgical operation when oral medication is not feasible. Reviewing the literature, he states that only a few fragmentary reports concerning the administration of digitalis by rectum have been recorded. The patients were twenty in number, ranging in age from 9 to 62 years. Nineteen had auricular fibrillation and one patient ectopic auricular tachycardia. The latter occurred in a girl, aged 9 years, whose case was diagnosed rheumatic fever, mitral stenosis and insufficiency and pericarditis with effusion.

Retardation in ventricular rate occurred in every instance. The average time necessary for an unmistakable initial effect on rate was two hours and thirty-five minutes. The average time which elapsed before a maximal effect on rate was apparent was nine hours and thirty minutes.

A desirable therapeutic effect was apparent in every instance. A characteristic change in the T-wave of the electrocardiogram occurred in fourteen of the nineteen observations. In five cases, although the rate was slowed, no T-wave change was observed. The initial effect was seen, on an average, in two hours and thirty minutes. The author gives a comparison of the rapidity of digitalis action when the drug is administered in large single doses by mouth, with that observed when it is given by rectal administration; he concludes that the lapse of time necessary for the occurrence of initial and maximal effect on the heart rate in patients with auricular fibrillation, when digitalis is given by mouth, closely approximates that required for the occurrence of similar effects when the drug is given by rectum. No observations on the duration of effect were made. Rectal therapy being regarded as an emergency measure the duration of action was not considered relevant to the problem. Three cases are cited in detail, and a comprehensive table of clinical summary of the twenty cases studied.

A STUDY OF MIXED LEUKEMIA WITH THE REPORT OF A CASE. RUDOLPH C. LOGEFEIL, Arch. Int. Med. **33**:659, 1924.

This condition occurred in a girl, aged 3 years. The true nature of the case was not recognized until blood smears were made.

The author emphasizes the point that the diagnosis of leukemia should not depend on the blood findings alone. The case should be considered as a whole, including the clinical picture as well as the histologic study of the various organs. This he has done in his case.

Two important points are stressed in his study, namely that myeloid and lymphoid cells were present at all times, the myeloid predominating early in the condition and the lymphoid predominating near death.

Arguments in favor of his opinion and his findings, as well as those against such conclusions set forth by other observers on similar findings, are given by the author at length; together with a summary of the three prevalent theories regarding the cause of mixed leukemias.

His article is concluded with twelve points, observations on his own case; the last two being that "no new observations were made relative to the real cause of the simple or mixed form of leukemia," and that "another case of a true mixed form of leukemia is added to a small number of previously reported cases."

A Hitherto Undescribed Form of Valvular and Mural Endocarditis. Emanuel Libman and Benjamin Sacks, Arch. Int. Med. **33**:701, 1924.

The purpose of the article as given by the author is a discussion of a group of cases belonging to the type of "the atypical verrucous endocarditis," so-called because of the unusual character of the endocardial lesions and their verrucous appearance, which they believe represent a hitherto undescribed form of endocarditis. The reason for this belief is based on the detailed and critical study of four cases which came to necropsy and two cases living and still under observation. The four cases reviewed in their entirety occurred in three females and one male, the ages ranging from 10½ to 37 years.

In each instance, there were peculiar valvular lesions, which differed in morphology and localization from those generally encountered in subacute bacterial rheumatic and other forms of endocarditis. The vegetations were free from demonstrable micro-organisms, and attempts to grow bacteria from the blood proved unsuccessful, despite the employment of methods which gave positive results in the greatest majority of cases of subacute anhemolytic streptococcus (and *Bacillus influenzae)* endocarditis. The authors believe with a better understanding of this entity, a more satisfactory terminology will doubtless ensue.

There is a summarized comment of each case, calling attention to the outstanding features which made up the clinical picture, a brief discussion of differential diagnostic points relating it to some known endocardial entity, and finally the characteristic necropsy findings of the peculiar valvular mural lesions which characterized the atypical form of endocarditis.

A full discussion of this entity is given under the subheadings of: Morbid Anatomy, Clinical Findings, Differentiation from Subacute Bacterial and Rheumatic Endocarditis, Etiology, Diagnosis and Prognosis. Under Diagnosis one reads: "In the presence of fever, arthritis, cardiac murmurs, pericarditis, white-centered petechiae, skin rashes of the character described (that is, erythematous and purpuric rashes) and repeatedly negative blood cultures, the diagnosis should present no difficulties. It seems highly probable, however, that cases will be encountered in which endocarditic phenomena will be masked by other symptoms." The authors cite such a case in their series in which endocarditic phenomena were not demonstrable during life but were confirmed by necropsy findings; another such case is now under observation.

A general summary concludes the paper, the outstanding points are briefly: A uniform finding was the extension of the endocarditic process from the ventricular aspect of the posterior cusp of the mitral valve along the adjacent mural endocardium of the posterior wall of the ventricle. Isolated areas of mural endocarditis were found in the right auricle and both ventricles. The vegetations were free from demonstrable bacteria and presented a histologic structure which differed in many respects from that of the lesions in other types of endocarditis.

The disease, in the form in which it attacked young people who previously had no organic symptoms, ran a subacute course with fever and progressive anemia.

Attention was directed to the similarity of certain of the symptoms to those observed in the erythema group of Osler and to the existence of a possible relationship between certain instances of the latter and the atypical form of endocarditis. The frequency of the disease and the ultimate outcome of non-fatal cases is a matter of conjecture. The etiology is as yet unknown, and the authors suggest that in future studies, the special methods adapted for a cultivation of filtrable viruses and spirochetes be employed among other methods in the search for the exciting agent.

LOEBER, New Orleans.

FUNCTIONAL DIASTOLIC MURMURS IN THE AORTIC AREA AND PISTOL SHOT SOUNDS IN THE GROINS IN INFANCY AND CHILDHOOD. JOHN LOVETT MORSE, Arch. Pediat **41**:559, 1924.

The author points out that in severe anemias one often encounters diastolic murmurs in the aortic area which are in fact not organic, as they clear up when the anemia improves, but are due to the lowered muscular and nervous tone produced by the anemia, and due to a relative insufficiency of the aortic orifice from dilatation.

For the same reason a pistol shot sound in the groin is often heard in severe anemias which disappears when the anemia improves. The sound presumably depends on a lowered vasomotor tone. Further proof of this is that the same pistol shot sound is heard not infrequently in other conditions in childhood which are accompanied by lowered vasomotor tone, such as pneumonia and typhoid fever. It is important, therefore, not to mistake these functional signs for organic lesions of the heart and thus render a mistaken diagnosis and prognosis.

VON MEYSENBUG, New Orleans.

FURTHER OBSERVATIONS ON SICKLE CELL ANEMIA. V. P. SYDENSTRICKER, J. A. M. A. **83**:12, 1924.

Sickle cell anemia is a familial and hereditary disease showing no sex preference and probably confined to the negro race. It is probably a defect of the spleen and the blood forming organs, with a resulting change in the erythrocytes which predisposes to hemolysis and phagocytosis. Anemia, when present is the result of excessive blood destruction, activated by factors that in a normal person would be innocuous. There are certain resemblances between this disease and familial hemolytic icterus.

The disease presents itself in two phases: the latent, in which symptoms are few, physical signs only suggestive and special methods of blood examination necessary for its recognition; and the active, in which the symptoms are rather constant. Dyspnea, palpitation and weakness are always present. Muscle and joint pains occur frequently. There are attacks of nausea and vomiting associated with abdominal distress. There is low fever and frequent night sweats.

Physically, the patient is poorly nourished. The sclerae are green-yellow, mucous membranes are pale. There is general lymphadenoid hyperplasia. The legs show ulcers or the scars of ulcers and edema.

In the active phase, the red cells are reduced to the neighborhood of two millions, with proportionate reduction of hemoglobin. There is marked leukocytosis averaging 20,000. The morphology is specific, many sickle cells are present in smears and in fresh preparation. There is also marked poikilocytosis with many microcytes and fragmentary forms. There are many normoblasts; megaloblasts are rare; nucleated sickle cells have been observed. Polychromasia is common but stippled basophilia is seldom seen. Phagocytosis is always demonstrable.

The pathology in general is interpreted as: (1) a peculiar change in the erythrocytes which causes them to assume bizarre forms, the so-called sickle cells; (2) an ability of these cells to penetrate the reticular tissues of the bone

marrow and the pulp of the spleen, perhaps even the walls of the splenic arterioles: (3) increased erythrocyte destruction most marked in the spleen. In the spleen there is found an exceedingly large amount of pigment. Pigment is also found in excess in the liver; and it can be found in the endothelium of the capillaries of various organs, especially in the collecting tubules of the kidneys. The pigment, with the exception of that found in the spleen, is iron free.

THE USE OF SULPHARSPHENAMIN IN VINCENT'S ANGINA AND STOMATITIS IN CHILDREN. LOUIS H. BARENBERG and MAX W. BLOOMBERG, J. A. M. A. **83**:25, 1924.

In fifteen cases of Vincent's angina, eight were treated by intramuscular injections alone and seven by intramuscular injection combined with local application of sulpharsphenamin three times daily. The dose was 0.1 or 0.2 gm. The average duration of disease in those patients who simply were injected was six and one-half days; of those on combined treatment, about four days.

The treatment was likewise found valuable in cases of stomatitis, and it is reported by the authors' colleague, Dr. Julius Blum, that pyorrhea alveolaris was definitely helped through three injections of 0.3 gm.

HENN, Chicago.

BOTULISM IN OREGON. FREDERICK D. STRICKER; WILLIAM LEVIN, and R. L. BENSON, Northwest Med. **23**:316 (July) 1924.

The authors describe an epidemic of botulism occurring in a family of twelve adults and children with 100 per cent. fatality. The family partook of home canned string beans, and within from seventeen to 116 hours afterward were taken ill. The duration of the illness was from ten to seventy-two hours. The symptoms were vomiting, a burning sensation in the throat, labored breathing, difficulty of swallowing, thick glairy mucus in the throat, absolute constipation, retracted abdomen, strabismus, dilated pupils, double vision and photophobia. The breath had the odor of spoiled cheese. Necropsies of three of the patients showed hyperemia of most of the organs and fatty chains of the liver. Three jars of the canned beans showed the *Clostridium botulinum;* the beans in these jars had a markedly putrescent odor. The juice of the spoiled beans was found to be extremely toxic to laboratory animals. The *Clostridium botulinum* was demonstrated in the soil in which the beans had been grown and an epidemic of limberneck in chickens had been reported from the same farm the year before. The authors suggest greater care to accomplish complete sterilization in home canning and recommend the use of a pressure sterilizer and boiling of the food immediately before use. They warn against the tasting of foods which seem to be spoiled. Polyvalent antitoxin should be given as soon as it is known that toxic food has been eaten.

SCOTT, Philadelphia.

CHRONIC HEART DISEASE IN CHILDREN WITHOUT RHEUMATIC FEVER. HUGH MCCULLOCH, Southern M. J. **17**:639, 1924.

Attention is called to a group of children who have chronic heart disease, but who do not show rheumatic fever and practically no lesions about the joints. The condition may be observed as early as the age of four or five years.

The predominating symptom is manifestation of fatigue. There is always a history of bad environment, repeated colds and upper respiratory infections.

The changes in the heart principally involve the myocardial tissue. There may be moderate cardiac enlargement but few valve changes. The children present important signs of infection in the nose, paranasal sinuses and tonsils. Tonsillar infection is always present, but may at times be secondary to infection in the paranasal sinuses or other parts of the nose. There is usually an excess of purulent secretion in the nose and nasopharynx. The maxillary sinus is most frequently infected.

It is probable that some poison, either bacterial toxin or some other by-product of the infection in the nose is liberated into lymph spaces and produces effects on specialized tissue such as the heart, kidney or brain. Marriott and Clausen have shown that such effects can be brought about by alterations in the physiochemical equilibria of body cells and fluids.

The treatment of this condition consists primarily in adequate treatment of the nasal structures and tonsillectomy. With adequate treatment these patients always tend to recover.

SCHLUTZ, Minneapolis.

Nervous Diseases

STUDIES ON THE PATHOLOGIC CREATINURIA OF INFANCY. GINO FRONTALI, Riv. di Clin. Pediat. **22**:29, 1924.

Frontali distinguishes two types of pathologic creatinuria in children according to whether or not the excretion of creatin is influenced by the administration of sugar. If sugar is administered to children suffering from chorea the pathologic excretion of creatin may be stopped, the endogenous metabolism may be spared and the child will gain weight although the choreic movements persist unaltered. The same result cannot be obtained through the exhibition of isodynamic quantity of other foodstuffs.

On the other hand, the sugar does not have any influence on the creatinuria of poliomyelitis or pseudohypertrophic muscular dystrophy.

A CONTRIBUTION TO THE STUDY OF THE MYOPATHIES OF EARLY INFANCY. GENNARO FIORE, Riv. di Clin. Pediat. **22**:606 (Sept.) 1924.

Fiore reports in detail the results of the clinical and pathologic study of a case of general muscular hypotonicity with progressive atrophy of certain muscle groups. Such cases he believes may be related to myatonia congenita, (Oppenheim's disease) and he thinks that in infants muscular atrophy and amyotonia may be the results of the action of the same morbific agent.

He finds a primary muscular deficiency in this case which was a fatty infiltration of the myofibrils in the atrophied and the hypotonic muscles localized in the anisotropic disc. Since this is said to be a product of the activity of the mitochondria of the myoblast, Fiore suggests a deficiency of the latter in the affected tissue as the primitive pathologic basis for the diseases in question.

SHIPLEY, Baltimore.

ROSENOW'S SERUM IN PREVENTION OF PARALYSIS IN ANTERIOR POLIOMYELITIS. FLOYD CLARKE and ANDREW G. DOW, J. A. M. A. **83**:421, 1924.

The authors report six cases in which they made the diagnosis of poliomyelitis; Rosenow's serum was given. In one case the patient developed a flaccid paralysis of the right leg and arm, but recovered without paralysis as did all the other patients.

HENN, Chicago.

SYMPTOMS AND HOME TREATMENT OF MENTALLY DEFECTIVE INFANTS AND YOUNG CHILDREN. JOHN THOMSON, Edinburgh M. J. **31**:285 (May) 1924.

In infancy, the symptoms of mental deficiency are the most interesting, the diagnosis the most difficult and treatment the most likely to be of value. Comparatively little has been written concerning the subject at this age. Thomson's material is obtained from 1,200 children, 952 of these under 5 years of age, many followed up for years. Classification into grades such as idiots, imbeciles and feebleminded while useful in older children is of little benefit in babies, though of interest. He thinks Tredgold's classification from the pathologic and clinical standpoint is the best. Thomson treats the subject from the point of view of the medical man in general practice, who has a better chance

of studying these children early than has the hospital physician. The mother is the best one to train and carry out the treatment and she needs the enlightenment of the family doctor, to whom she can give many valuable points in the history of both family and infant. On examination there will be found abnormalities in appearance of the head, in behavior, in easily recognized causative diseases, in occurrence of epileptiform seizures, especially petit mal. The physical development and the use of the senses of the normal infant is considered as the basis for comparison with the infant whose healthy growth has been delayed, deficient or absent. Constant discontented crying, bad habits (somatopsychosis of Leonard Guthrie), disturbances in speech, late control of the bladder and bowel are unpleasant symptoms often occurring in mentally deficient babies. The child is not and may never become like other children.

In the treatment it is best at first not to cause the mother further distress by unnecessary emphasis on the full gravity of the condition, until she gives the physician her confidence in his opinion and guidance. Thomson thinks that parents may be spared much distress when the infant dies early without their realization of the defects. Making the outlook hopeless is of no value to the mother, to whom the physician must look for training and care if the child is to improve. The present progress is of more importance practically than the future. Thomson has written a small book: "Opening Doors" for the instruction of educated mothers to be used in training such infants. Simple actions must be taught, as must the natural desire to please his mother, bad habits must be checked, observations encouraged, speech learned, the character developed and the body functions controlled. In spastic paralyses Thomson advises detailed passive movements of the stiff joints, and the exercise of the child's will in overcoming the muscular stiffness. Massage at this age is of little help, likewise electricity, but operations on the muscles and tendons are sometimes beneficial. The state of the bodily health must be cared for.

The author concludes by urging the prevention of birth injuries to the brain, and improvement in obstetric practice, which in Edinburgh originated from the work of Ballantyne.

NEFF, Kansas City.

POSITION REFLEXES IN INFANCY. Z. LUCIANO MAGNI, Riv. di clin. Pediat. **22**:237, 1924.

The author understands by position reflexes the condition of tonic contraction in certain muscles about a joint when the latter is moved passively, which fix the joint in the new position for a short time. For example, if the foot is dorsiflexed and internally rotated contraction of the tibialis anticus delineates the tendon on the skin. This muscular contraction is maintained holding the foot dorsiflexed and in internal rotation for a short time after release of the foot. Luciano believes these reflexes to be an expression of those by which upright posture is maintained and that they proceed along the motor extrapyramidal tract.

They show themselves in the same way in children and adults but are absent during the first year of life.

SHIPLEY, Baltimore.

Diseases of the Eye

REPORT OF A CASE OF CHLOROMA OF THE ORBIT. CYRIL BARNERT, Arch. Ophthal. **53**:454, 1924.

Barnert reports a case of chloroma of the orbit in a child, aged 2 years. A complete physical examination and differential blood counts established the diagnosis of acute myeloblastic leukemia. Two months after onset of ocular symptoms the child died. Necropsy confirmed the diagnosis. An extensive bibliography is appended.

WESCOTT, Chicago.

Diseases of the Nose and Throat

ANOMALIES IN LARYNGOLOGY. SAMUEL M. D. COHEN, M. J. & Rec. **120**:223, 1924.

CASE 1.—The patient came for a tonsillectomy. Examination was practically negative except that behind each posterior pillar, and running parallel to them a pulsating vessel was noted. The size of the pulsating vessel was about that of an ordinary lead pencil. It could be traced to a little above the soft palate, then seemed to disappear outward and forward.

CASE 2.—This patient, aged 10 days, was one showing a supernumerary tongue. The child was almost continually cyanotic. The difficulty in breathing was noted immediately after birth and seemed to be principally on inspiration. The breathing became easier when the head was held down. Examination of the throat showed a peculiar body lying in the pharynx, more toward the left, parallel to the long axis of the pharynx. Breathing caused it to move either up or down or to slip over the tongue, bringing itself into plain view. It was removed as near base as possible. Specimen sent to pathologist. His report showed gross and microscopic appearance of a tongue.

The child is now 1 year old and in perfect health.

IS TONSILLITIS MERELY A SYMPTOM? SAMUEL M. WILSON, M. J. & Rec. **120**:209, 1924.

The author states that like many others, he was very enthusiastic about the brilliant results that appear to follow tonsillectomy in some cases of chorea, rheumatism and allied disorders, but these results do not always stand critical study nor the test of time. Articles are becoming numerous and opinion outspoken in regard to this, pleading for care in diagnosis and more attention to the sinuses, ears and septal deflections, before assuming that the primary trouble lies in the tonsils, even though these may appear somewhat large.

Treatment of the nose is usually required, in addition to that of the tonsils, and if well performed will in most cases, render a tonsil operation superfluous.

Like all operative procedures, tonsillectomy has its place, and should only be performed when necessary, after a careful, discriminating diagnosis.

KINBERGER, New Orleans.

A RARE CASE OF MALFORMATION OF THE NOSE. IRENE MENYHÁRD, Jahrb. f. Kinderh. **106**:128, 1924.

This child was born with three nares, one of which did not communicate with the nasal cavity.

SUTHERLAND, Chicago.

Diseases of the Skin

SIGNIFICANCE OF THE DEVELOPMENT OF PIGMENT IN HELIOTHERAPY. HANS JANSEN, Ugesk f. Laeger **31**:584, 1924.

The hypothesis held by Professor Bang that heliotherapy is most effective in people who show abundant pigmentation is at variance with the observations made by the author. Jansen still believes the significance of the pigment to be in its protective qualities against light and especially the ultraviolet rays; and that the rays which are most injurious have a tendency to produce the greatest activity in the protective agencies of the organism.

While there may be an advantage in abundant pigmentation, nevertheless, the reason that blonds do not have development of the skin equal to that of of brunettes is dependent on the fact that they cannot resist the same light intensity without a tendency to burn instead of an increased pigmentation.

As proof that pigmentation is not the deciding factor as to the benefits derived from heliotherapy in tuberculosis, the author cites the fact of the

intense pigment produced by the mercury quartz lamp treatment as contrasted with the golden brown skin developed in mountainous regions. The beneficial results are much greater with direct exposure to sunlight at higher altitudes and are not dependent on the amount of pigment in the skin.

In view of the foregoing observations, the frequency of rachitis in negroes may be considered to be due, in part, to an inability of the ultraviolet rays to penetrate the pigment layer, so that their beneficial influence on the mineral metabolism is lost.

BESNIER'S PRURIGO WITH ASTHMA. KAJ BAAGOE, Ugesk. f. Laeger **33**:609, 1924.

In 20 per cent. of the children suffering from asthma, Besnier's prurigo occurs as a complication. This disease begins, as a rule, in the first year of life, often during the third to fourth months, as a simple undifferentiated eczema of early childhood affecting the scalp and face.

The close relationship between Besnier's prurigo and infantile eczema is indicated by the symptoms they have in common as: intense itching, stubbornness to treatment, positive skin reactions, changes affected by various diets, and a course of periodical exacerbations and remissions.

All patients under observation had positive skin reactions, indicating an anaphylactic disposition for one or more of the organic substances tried. Consequently, the author concludes that Besnier's prurigo may be considered as a symptom of an anaphylactic reaction.

The prognosis in patients suffering from Besnier's prurigo is considered good in that there is a tendency to a spontaneous cure.

ICHTHYOSIS IN TWIN BROTHERS WITH GRAEFE'S SYMPTOM AND ACROMEGALIC GROWTH DISTURBANCES. EGGERT MØLLER, Ugesk. f. Laeger **35**:639, 1924.

Twin brothers showing growth disturbances during puberty similar to the changes found in acromegaly are reported.

Early history of these patients gives evidence of a retarded physical development, the presence of a congenital ichthyosis, and a tendency to exudative diathesis.

Roentgenograms showed no changes of the sella turcica, but did show an increased shadow in the region of the sphenoidal sinus.

Prognosis is reserved. The giving of thyroid extract may temporarily improve the skin condition. Roentgen-ray treatment of the sphenoidal area may be considered.

SCHLUTZ, Minneapolis.

Surgery and Orthopedics

APPENDICITIS AND THE APPENDICOPATHY CAUSED BY OXYURIS. ARTUSI, Riv. di clin. Pediat. **22**:392, 1924.

Artusi discusses the biology of Oxyuris in relation to its location in the cecum and appendix. These worms are frequently found in the appendix and as a rule produce no symptoms. Appendicitis when it occurs, is due to secondary infection and is very rare. Oxyuris may produce an appendicopathy of greater or less intensity directly which simulates appendicitis, with localized or colicy pain or uneasiness in the ileocecal region. This condition cannot always be diagnosed, but should be considered if the local signs on examination are not sufficiently severe to correspond with the symptoms, e. g., easily palpable abdomen with little rigidity, muscle spasm or tumefaction. In such a case, knowledge of infection with the worms makes the diagnosis likely. It should be specially thought of in children when appendicitis-like symptoms are complained of without marked elevation of temperature or change in the

pulse. Eosinophilia is a point in favor of the diagnosis of oxyuric appendicopathy. These children may have sensations of weight or tension in the iliac fossa and sometimes periumbilical pain.

Prognosis is good and treatment is by anthelmintics and purgatives.

SHIPLEY, Baltimore.

ACUTE OSTEOMYELITIS OF SPINE. K. PATERSON BROWN, Edinburgh M. J. **31**:360 (June) 1924.

The disease is rare, sometimes unrecognized, especially early. Brown reports a boy, aged 10 years, suddenly developing shooting pain in the left lumbar region and left iliac fossa, disappearing on lying down, later weakness in the left leg, and pain in hips, extending to disability in both legs; the back muscles became rigid, the temperature and pulse raised, and other evidences of toxemia. On the sixteenth day, when admitted to the hospital, there was a large oval fluctuating swelling to the left of the spine from the eleventh dorsal to third lumbar vertebra, prominent local veins, exaggerated left knee jerk and a slight ankle clonus. The opening of the abscess showed the pus coming from the sides of the bodies and transverse bodies of the upper lumbar vertebrae, from which loose portions of bone were removed. The culture was *Staphylococcus aureus*. The recovery in a month was without complication.

Another boy, aged 10 years, had fallen six days before, suffering trauma to his back, and was brought into the hospital with fever, pain and rigidity in lumbar region, when a fusiform swelling, fluctuation, and tenderness were present. No primary disease existed elsewhere in the body. When the pus was drained, an opening was found in the lumbar aponeurosis leading to the lamina of the second right lumbar vertebra. No sequestrae were found. This culture was also *Staphylococcus aureus* and the wound was healed in about one month.

Acute osteomyelitis is usually due to the staphylococcus and may involve any part of the spinal column, more frequently the lower and any part of the vertebra, though the infection of the body is more serious for spreading, especially when the veins are involved developing into pyemia or meningitis. Superficial pointing from the vertebral processes is the more favorable location.

Young children, especially boys, are more often the victims with a history of trauma or a septic focus. Pain at first localized in the infected spine is the most prominent symptom throughout the disease. Progressive toxemia is in evidence. Lumbar puncture is of no help in diagnosis, unless meningeal symptoms are present. Abscess appears about ten days after onset. Meningitis is hopeless. Retention of urine and abdominal pain are present in some cases. A roentgenogram is negative in the early days.

Early drainage, removal of sequestrae, in severe cases drainage of psoas abscesses, laminectomy if necessary comprise the treatment. In the 40 per cent. of recoveries the restoration to normal is rapid and complete as to function.

NEFF, Kansas City.

MORTALITY FROM EMPYEMA IN CHILDREN. WM. E. LADD, and GEO. D. CUTLER, Surg., Gynec. & Obst. **39**:429, 1924.

Empyema in children is quite different from that in adults. From a study of 268 patients operated on by the authors the following important facts were elicited:

1. The mortality of infants from pneumonia even without the complication of empyema is very high, ranging between 50 and 75 per cent. the first year and 30 and 40 per cent. the second year.

2. The type of infection has a direct bearing on the mortality, the streptococcus being more often fatal than the pure pneumococcus or mixed infections.

3. The mortality from empyema is very high if operation is performed early. Thoracocentesis should be done as a temporary measure until the pneumonic process has subsided.

4. Forty-two of the 268 patients were operated on by the closed method, inserting a tube through a cannula introduced between the ribs. The mortality was 28 per cent. The pleural cavity was irrigated with surgical solution of chlorinated soda or ox bile, and 50 per cent. required a secondary operation to provide more adequate drainage or to allow the lung to expand.

5. Rib resection was done on 226 patients, with a mortality of 15.9 per cent. and only 4 per cent. required any type of secondary operation to hasten obliteration of the cavity.

6. Gas and oxygen anesthesia is very adaptable to empyema cases because it avoids the undesirable complications of ether and allows for hacking up of pleural adhesions, a step which cannot be carried out with procain alone.

7. Secondary pneumonia was the commonest cause of death in empyema.

MILLER, Chicago.

Miscellaneous

THE HUMAN THORAX CONSIDERED AS A RESONATOR. G. E. BUSHNELL, Arch. Int. Med. **33**:763, 1924.

A dissertation on the acoustics of the thorax and organs of respiration is given by the author, who goes thoroughly into the similarity of the physics of many familiar resonators and points out their similarity and dissimilarity to the normal thorax. He states that the latter differs from all other resonators in two respects; first, the solid parts of its contents are largely under a certain tension, secondly, it is what might be called a compound resonator.

The article is full and comprehensive on sound production and transmission in the thorax; the author believes the phenomena observed in the physical diagnosis of the diseased lung depend largely on the impairment or destruction of the insulating parenchyma with impairment or loss of its specific vibratility and consequently, with improved transmission of bronchial sounds. In general, the transmission, not the character of breath sounds is altered in disease.

LOEBER, New Orleans.

UROLOGICAL LABORATORY PROCEDURES. LOUIS NERB, M. J. & Rec. **120**:217, 1924.

Urine specimens showing a great many pus cells, with no organism, are directly examined for tuberculosis, before the guinea-pig is injected. The urine is allowed to stand in the test tube overnight so that the sediment settles down gradually. The supernatant fluid is carefully decanted and smears are taken from the upper layer of the sediment. The reason for taking the upper part is that the tubercle bacilli are lighter than the pus cells and other solids that are found in the urine. Care should be taken that the lumen of the catheter should be free from antiseptics, such as weak formaldehyd solution, as this will inhibit the growth on culture media, particularly with *B. coli* infections. The author stresses the fact that urine containing large numbers of pus cells is always suggestive of tuberculosis.

KINBERGER, New Orleans.

APPLICATIONS OF BIOMETRY TO THE FIELD OF PEDIATRICS. G. FRONTALI, Riv. di clin. Pediat. **22**:250, 1924.

This article contains nothing new, it is a general discussion of biometry in its broadest sense, in its application to pediatrics. The author points out that this is a particularly fertile field for biometric studies of all types, since it is through biometric data that we are able to identify normal or abnormal development. A discussion of the various technical methods and their application follows.

CONCERNING A MODIFICATION OF THE SYSTEM OF CHILD ANTHROPOMETRY. G. DEL DUCA, Riv. di clin. Pediat. **22**:229, 1924.

The writer proposes a new table of measurements according to the anthropometric method of Viola for the estimation of "constitutional evolution" (physical development). These tables give the value of different body measurements from birth to adult life (45 years) so that growth may be estimated every half year for comparison with normal growth rhythm. Values were controlled by the author with numerous observations.

OBSERVATIONS ON THE CEPHALIC BRUIT. PAOLO ROTONDI, Riv. di clin. Pediat. **22**:361, 1924.

Ascultation of the head during early life often demonstrates a cephalic whistling sound, systolic in time and more intense during inspiration. The same sound may sometimes be heard over the heart but is less intense. It is diminished by lateral inclination of the head and by increased intracranial pressure. It probably is a venous hum, rises in the jugular and in cases of severe anemia is reinforced by a bruit in the great cerebral veins. It is normally audible from the age of 6 months to the end of the second year, in some pathologic conditions from the beginning of life to the fourth or fifth year. Its persistence and increased intensity are important symptoms of anemia, and its diminution and disappearance may be of diagnostic value in determining the existence of increased intracranial tension.

INFANT MORTALITY IN CAGLIARI, 1917-1922. ANTONIO CARDIA, Riv. di clin. Pediat. **22**:527, 1924.

Mortality among the children up to the age of 12 years in Cagliari during the period of this study was 6.58 per thousand of the population, the greatest number of deaths occurring during the first year of life. Sixty-one and one-fourth per cent. of the deaths were the result of prematurity, "congenital debility" and diseases of the digestive tract.

SHIPLEY, Baltimore.

Book Review

AN INTERNATIONAL YEAR BOOK OF CHILD CARE AND PROTECTION. By EDWARD FULLER, with an Introduction by PERCY ALDEN. Longmans, Green & Company, New York, 1924, 448 pages, price, $2.50.

This book is a very exhaustive and concise compilation of facts concerning the state and voluntary effort for child welfare throughout the world. Each state, great and small, is included and the main projects carried on by the communities listed. It is a very valuable, in fact necessary reference book for one who would have an idea of the work which is being done for children throughout the world.

It is surprising how much information has been put into this one volume, and one cannot but commend the industry and patience which were necessary for the compilation of such an array of facts.

News and Comment

Dr. J. P. Crozer Griffiths is retiring from the professorship of pediatrics of the medical school of the University of Pennsylvania. He has been succeeded by Dr. J. Claxton Gittings.

Society Transactions

CENTRAL STATES PEDIATRIC SOCIETY

Rochester, Minn., Oct. 30, 1924.

E. J. Huenekens, M.D., *President*

Congenital Webbing of the Neck in Sisters. Presented by Dr. J. M. Frawley.

Two cases of congenital webbing of the neck in sisters were reported. Each had a fold of skin extending from the acromion process to the mastoid on both sides. The skin was soft and pliable, nothing but skin being included in the fold. No muscle was present. The chins were of the drooping type; the back of the head was flat. The hair came well down from the mastoid toward the shoulder. One sister also showed webbing of the axillae. The roentgenogram of this case revealed rudimentary cervical ribs, but in both sisters, so far as could be determined, there was an absence of two cervical vertebrae. The condition, as indicated by the literature, is very rare.

Trophic Changes of the Nails in Bronchiectasis. Presented by Dr. M. G. Peterman.

Photographs were presented of patients with bronchiectasis, whose finger and toe nails showed clubbing. In contradistinction to these typical changes, pictures were shown illustrating trophic changes of the nails in children with bronchiectasis. The photograph shown here gives a good idea of the condition.

Trophic changes in finger nails.

THE STANDARDS OF BASAL METABOLISM OF CHILDREN. Presented by DRS. I. SANDIFORD and E. R. HARRINGTON.

An investigation on the basal metabolism of the school children of Rochester is being carried out, in order to establish with greater accuracy the normal standard for persons between the ages of 5 and 20 years. The children come to the laboratory at 7:15 in the morning without breakfast, and are allowed to rest half an hour before the expired air is collected. The gasometer method with analysis of the expired air is used, according to the technic fully described elsewhere by Boothby and Sandiford. Single determinations are done on three successive days, except in a few cases where it has been possible to obtain only one or two determinations. The surface area is determined by the DuBois height-weight formula, and the heat production plotted according to calories per square meter.

The study is not yet complete, sixty-six girls and sixty-seven boys having been tested up to the present time, but there seems to be a remarkable consistency in the results obtained. It seems justifiable to state that the natural metabolism of children is quite as consistent and stable as that of adults.

THE PATHOLOGY OF HUMAN PYELITIS. Presented by DR. H. F. HELMHOLZ.

Lantern slides of gross and microscopic sections of the kidney were presented, to show the changes due to hematogenous and ascending infection of the kidney. Although there were distinguishing features in the various specimens, no definite conclusions could be drawn as to the mode of infection.

CASE REPORT. BACILLURIA WITH UNUSUAL SYMPTOMS. Presented by DR. E. B. BOYD.

Two cases of bacilluria without definite symptoms or the usual signs of urinary infection were presented. The first patient was a girl, aged 12 years, who came to the Mayo Clinic with a history of stomach trouble. She had had a pain in the lower abdomen with occasional regurgitation. There had been a slight vaginal discharge. Examination showed a slight vaginal irritation and the urinalysis revealed a trace of albumin and a few pus cells. The latter were suggestive of a mild urinary infection, and on culturing a catheterized specimen, many colonies of colon bacilli and staphylococci were found.

The second case was a girl, aged 4 years, who came to the Clinic because of an irritation of the vulva. Her general health was excellent, but because of the history of spells of frequency and the fact that the urine showed a few pus cells, it was thought best to culture a catheterized specimen, which revealed many colonies of colon bacilli.

In both cases the routine of the examination was essentially negative, and only the cultured urine revealed the presence of the urinary infection. The usual treatment of forced fluids and urotropin was instituted in each case and the urine became sterile in a very short time. Clearing up the infection has relieved the symptoms in both patients.

THE PRESENCE OF DIPHTHERIA BACILLI IN THE NASAL CAVITY OF THE NEW-BORN. Presented by DR. S. AMBERG.

In recent years there have been a number of reports from abroad, to the effect that so-called diphtheria bacilli are found in large numbers in the nasal cavity of the new-born infant. In a series of 421 cases, cultures being taken once in 182 cases and twice or more in 239, the incidence of the diphtheroid bacilli was 4.5 per cent.

ABDOMINAL TUMORS. Presented by DR. M. G. PETERMAN.

A review has been made of the 100 tumors of the abdomen seen in the Pediatric Section of the Mayo Clinic, in an attempt to find diagnostic points and to evaluate symptoms. There are fifty males and fifty females in this

study. The ages range from 6 months to 15 years, sixty-three patients being under 10 years of age. The series of cases is divided into two groups, the first of which contains the splenomegalies, and the second group all other types of abdominal tumors. There were thirty-six enlarged spleens; those associated with other generalized infections were not considered. In the second group thirty tumors involving the kidney, five cases of tuberculous peritonitis, three ovarian tumors and three fecaliths were found. The remaining twenty-three cases were quite unusual and offered problems in diagnosis. A careful study of the complete physical findings and the indicated laboratory tests makes a diagnosis possible in a high percentage of cases. However, there remain a certain number of abdominal tumors which cannot be diagnosed before exploration.

THE LAG IN GROWTH OF BACTERIA CAUSED BY A CHANGE OF REACTION IN THE MEDIUMS. Presented by DR. H. F. HELMHOLZ.

The theme of this talk is embodied in an article: "An Experimental Study of Therapeutic Procedure in Pyelocystitis," published in this issue.

CASE REPORT. PERINEAL DESCENT OF THE TESTICLE. Presented by DR. J. M. FRAWLEY.

This was a case of ectopic testis which was discovered during examination in the Mayo Clinic. The child was aged 10 months, and had a perineal swelling. The left side of the scrotum was empty and a diagnosis of perineal testicle was made. In order to explain the condition, it is necessary to understand the development of the organ. Such a testis does not function so far as spermatogenesis is concerned, but the interstitial function is unimpaired. The usual procedure is to replace the testicle in the scrotum before puberty. It is better to perform this operation as early as possible because of the danger of injury to the testicle. (This case will be reported in detail later.)

CHRONIC ULCERATIVE COLITIS. REPORT OF ADDITIONAL CASES. Presented by DR. R. L. J. KENNEDY.

Several cases of chronic ulcerative colitis have been seen in the Clinic since the report on the condition published a year ago by Helmholz. These patients came to the Clinic with the general complaint of frequent and bloody stools. Diagnosis was based on the history and on the roentgenograms of the colon and the proctoscopic findings. The pictures in ulcerative colitis are very characteristic; the absence of haustra in the colon being noticeable in almost every case. A patient who had returned after several months for re-examination was presented. This girl represented what has been an unusual result with medical treatment. She weighed 59 pounds (26.8 kg.) when she left the hospital and her weight on return was 100 pounds (45.4 kg.). The improvement was real as well as apparent, the roentgenograms showing the presence of numerous haustra.

Surgery must be considered in the majority of cases because of the refractory nature of the condition. The Brown operation, an ileostomy with both ends of the loop open so that continuous irrigation may be carried on, is the procedure of choice. Bargen has made cultures from lesions of patients with active ulcerative colitis, and has isolated a diplococcus which has produced very similar conditions when inoculated into animals.

THE KETOGENIC DIET IN THE TREATMENT OF EPILEPSY. Presented by DR. M. G. PETERMAN.

An earlier paper on the treatment of epilepsy in children by the ketogenic diet has appeared in this journal. No ill effects have been noticed in more than twenty-five patients, observed over periods ranging from six months to two years. Most of the children have gained weight and strength and have

made normal physical and mental development. Each diet prescription is an individual problem. The diet is not started abruptly, the carbohydrate and protein being reduced gradually while the fat is increased. Any tendency to vomiting or nausea is easily checked by the administration of orange juice. Immediate reduction in number and severity, or complete cessation of the attacks usually occurs as soon as the state of acidosis is established.

A boy, aged 8 years, who had been on the ketogenic diet for eight months, was presented. For the last five months he had been absolutely free from attacks.

THE EFFECT OF ATROPIN ON THE BLADDER. Presented by DR. S. AMBERG.

As yet there is no agreement as to whether atropin has an effect on the bladder. We have been working on enuresis cases and incidentally have found out some things about atropin. In our study we have paid attention to the effect on the pressure of the bladder at rest, the number of bladder contractions, as well as the height of the contractions. In some cases there is no doubt that atropin has an effect on the bladder. We have also studied the effect on the pulse rate. There seemed to be a definite initial diminution in the majority of the cases. Observations have also been made in regard to mydriasis, flushing and dryness of the mouth.

CORD BLADDER. Presented by DR. H. F. HELMHOLZ.

The term cord bladder has been applied to an interesting group of cases, in which the lesions of the bladder are similar to those associated with diseases of the spinal cord. Children without any obstruction of the urethra are unable to empty the bladder. Such a difficulty is a great handicap in clearing up any infection of the urinary tract. There have been nine such cases seen here at the Clinic in the last four years. The outstanding clinical feature is a suprapubic tumor which decreases with the passage of urine. The symptoms vary with the severity of the urinary infection. On examination, the urine contains large amounts of pus. Cystoscopic examination generally reveals a large bladder which may be sacculated cystic dilatation. The outlook in these cases is bad, because it is impossible to influence the infection except by catheterization to empty the bladder. As a result of the constant stasis we have ideal conditions for recurring infections. The possible transplantation of the ureter into the rectum, as is done in exstrophy of the bladder might be tried. A determination of the blood urea will indicate the extent of the kidney destruction.

CASE REPORT. ANGIOSARCOMA OF THE STOMACH. Presented by DR. E. B. BOYD.

A girl, aged 10 years, came to the Clinic complaining of bleeding from the bowels. Three years before she had had an attack of influenza, following which she had had an attack of high fever, accompanied by headaches, vomiting and tarry stools. At six month intervals there was a recurrence of the tarry stools with marked anemia.

The liver was palpable about 3 cm. below the costal margin, and there was definite tenderness just below the edge of the liver with pain radiating to the epigastrium. It was considered a case of duodenal ulcer and a gastro-intestinal roentgenogram showed a filling defect of the stomach, probably from an extrinsic mass. The tumor was palpable only when the patient was in standing position. The child was transfused and an exploratory operation performed. At operation, an angiosarcoma was found and about two-thirds of the stomach was resected. The patient has gained in weight and is at present in excellent health.

MELENA NEONATORUM WITH PATHOLOGIC FINDINGS. Presented by DR. R. L. J. KENNEDY.

This paper will be found in this issue.

STUDIES ON ISOLATED LOOPS OF THE INTESTINES. Presented by DR. S. AMBERG.

A series of experiments on isolated jejunal loops in dogs, prepared by a modification of the Wella method, were done. The average rate of secretion during hunger and after administration of food was determined. The figures denote the number of cubic centimeters an hour. In Dog 1 the hunger secretion exceeds that obtained after the administration of food, while in Dog 2 the opposite is the case, but after about six hours it is seen that the secretion reverts to the hunger type. The character of the secretion during hunger and feeding is somewhat different, the former containing more débris. The reaction of the fluid, determined at the opening of the fistula with neutral red paper, varied from a p_H of 8.2 to 8.9. Sodium, potassium, calcium magnesium, chlorin and phosphates were determined in the supernatant fluid and in the residue of the centrifugalized secretion. The most striking feature is that the residue contains more calcium than the supernatant fluid. The food secretion in one of the dogs on two occasions when the temperature was excessively high showed a diminution.

Experiments on Isolated Jejunal Loops

	Hunger Secretion						Food Secretion						
Hours	1	2	3	4	5	6	1	2	3	4	5	6	7
	cm.						cm.						
Dog 1	1.2	1.1	1.2	1.3	1.1	1.1	0.5	0.3	0.4	0.4	0.5	0.5	1.1
Dog 2	0.5	0.9	0.7	0.8	0.5	0.4	0.9	1.1	0.9	0.9	0.8	1.0	0.7

RECTAL POLYPUS. Presented by DR. R. L. J. KENNEDY.

A child was brought to the Clinic because of a mass protruding from the anus. This had been noticed since shortly after birth. It was said to bleed at times and caused painful defecation, so that frequent laxatives were necessary. On examination, a polypoid, pedunculated mass was found protruding from the anus. The proctoscopic examination could not be made because of the painful condition (but the note from the examining surgeon stated that there was a polypoid mass protruding from the anus, apparently rising from the coccygeal periosteum). The roentgenogram of the spine showed a congenital deformity of the sacrum, with a spina bifida occulta of the fifth lumbar vertebra. The child was operated on, and the polypus removed. According to the surgeon, the polypus apparently rose from a bony projection on the right side of the sacrum. A definite diagnosis was not made. A small amount of fluid was present after the removal of the mass, but the source could not be determined. Two days after operation the child's temperature rose to 106 F. (41.2 C.). Meningitis developed and lumbar puncture showed a mixed infection. Three days later the child died. At necropsy a defect of the anterior surface of the sacrum was found, measuring about 2 by 4 cm. From this emerged the cut edges of the spinal meninges, representing the base of an anterior sacral meningocele. This case will be reported in detail later.

CASE REPORT. UNILATERAL HYDRO-URETER AS A CAUSE OF CHRONIC PYELITIS. Presented by DR. E. R. HARRINGTON.

This child, aged 7 years, was brought to the Clinic complaining of pus in the urine. The presence of pus was first noticed when the child, aged 1½ years, was, during an attack of tonsillitis, in the course of a routine examination. Following the attack, the pus did not disappear. The tonsils were removed without effect on the infection.

Physical examination was negative except for slight tenderness over the kidneys. Urine cultures contained gram-negative organisms too numerous to

count. The phenolsulphonephthalein test was 50 per cent. The blood urea was 30 mg. per hundred cubic centimeters. Roentgenogram of the kidneys, ureters and bladder was negative except for bifurcation and right sided sacralization of the fifth lumbar vertebra. On cystoscopic examination, a turbid residual urine and chronic inflammation of the entire bladder mucosa was found. The left ureteral meatus was normal, discharging a clear urine and the right ureteral meatus was gaping, discharging a turbid urine. A pyelogram of the right side showed a dilatation of the pelvis and calices and a dilatation of the ureter in the upper and lower portions. A clinical diagnosis was made of right hydro-ureter and a hydronephrosis. At operation a very small kidney with double hydro-ureter was removed. About 75 per cent. of the kidney substance had been destroyed. The child made an uneventful recovery.

THE COAGULATION AND BLEEDING TIME IN THE NEW-BORN. Presented by DR. O. GROB.

The coagulation and bleeding time with and without administration of whole blood shortly after birth has been determined in sixty new-born infants. The methods used by Rodda were employed, and results in accordance with his were obtained. No marked difference has been found between the patients which received blood and those which were untreated. None of the sixty patients had a delayed bleeding time over thirty minutes, and none presented evidence of hemorrhage. In moderate icterus neonatorum, the average coagulation and bleeding time is the same as in other cases. With a pronounced coloration of the skin or blood serum, a delay in the coagulation time may be found. The bleeding time, though more frequently prolonged in jaundice as in nonicteric cases, did not show definite relation to the severity of the icterus.

FILTRATION OF PROTEIN SOLUTIONS. Presented by DR. S. AMBERG.

The work on filtration of protein solutions emanated from some studies with Dr. Rowntree, concerning the disappearance of definite amounts of fluid placed on porous surfaces. Alundum crucibles of a certain density were used, and the filtrations were done at the negative pressure of 30 mm. of mercury. Some interesting data were obtained concerning filtration pollution.

The rate of filtration of protein solutions of various concentrations was determined, the most striking being that solutions of mucin flowed much slower than corresponding solutions of other proteins. With a given protein solution there is a certain relationship between viscosity and rate of filtration, but blood serum with greater content of protein and a greater viscosity filters faster than a gelatin solution of lesser viscosity and lesser protein concentration. It is evident that viscosity cannot be the only determining factor in the rate of filtration.

HEXAMETHYLENAMIN THERAPY IN PYELITIS. Presented by DR. H. F. HELMHOLZ.

Considerable success has been obtained in treating patients with chronic pyelitis of long standing with urotropin. In those patients in whom we have not been successful, there has usually been an associated condition, such as congenital hydro-ureter, spina bifida or cord bladder. Even in these patients we have been able to influence the infection. Urotropin seems to be of particular use in those chronic cases of pyelitis where by a complete examination of the urinary tract any anatomic difficulties to the outflow of urine can be excluded. The urotropin treatment should be combined with the administration of as large amounts of fluid as it is possible for the child to take. The initial dosage of urotropin is generally 10 grains four times a day, increasing it to 15 and then to 20 grains. Ammonium chlorid in doses of from 10 to 30 grains, depending on the acidity which is desired, is used with the urotropin. The results obtained by such treatment certainly warrant its use in chronic pyelitis.

ST. LOUIS PEDIATRIC SOCIETY

Sept. 26, 1924

GEORGE M. TUTTLE, M.D., *President*

REPORT OF A CASE OF BOTULISM. Presented by DR. ADRIEN BLEYER.

A girl, aged 8, became ill the day following the eating of some spoiled sausage; indisposition or malaise with increasing muscular weakness was soon followed by inability to swallow. Constipation existed throughout the duration of the illness. When seen three days later the child was unable to move her extremities, raise her head or turn over in bed although all deep reflexes could be elicited. Pupillary signs were absent, sensorium undisturbed and the mind clear; there were no signs of meningitis. Because of the anhydremia, the result of involvement of muscles of swallowing she was sent to hospital. Laboratory examinations of blood, urine and spinal fluid were all negative. Death occurred a few hours after admission from respiratory failure. At no time was there any fever or pain. Necropsy revealed congestion of mucosa of stomach and small bowel, punctate hemorrhages of peritoneum and enlarged mesenteric glands.

REPORT OF A CASE OF ARACHIDIC BRONCHITIS, LUNG ABSCESS, AND PYOPNEUMOTHORAX. Presented by DR. PARK J. WHITE.

A girl, aged 2½ years, aspirated a peanut July 17. After the initial choking there were no symptoms except a cough, gradually increasing in severity. She was then seen by seven physicians, who prescribed for bronchitis and told the mother not to worry about the peanut. August 12, bronchoscopy by Drs. Short, Myers, and Payne resulted in the extraction of the peanut. Tracheotomy had to be done shortly afterward in order to aspirate the large amount of pus. This was followed by subcutaneous emphysema. August 26, when I first saw the patient, there were typical signs of left pneumothorax, and in a few days, signs of pyopneumothorax. After aspiration of pus, intercostal drainage was resorted to, to prevent pressure on the mediastinum by pus and imprisoned air. Efforts at improving the general conditions, including nasal feeding, were unsuccessful, and the child died September 12. Necropsy revealed fibrinopurulent pericarditis, left empyema without accumulation of free pus, left lung collapsed and bound to the diaphragm. Instead of one large abscess in the collapsed lung, there were many miliary abscesses, one of which, near the diaphragm, had ruptured into the pleura.

SYMPOSIUM ON SPASTIC PARAPLEGIA. NEUROLOGIC AND PATHOGENIC ASPECTS. Presented by DR. LELAND B. ALFORD (by invitation).

The clinical types of infantile cerebral paralysis usually found are paraplegia without involvement of parts above the waist, and diplegia with spasticity of the legs and athetoid movements of the arms and face. There are also flaccid types, and rarely types in which chorea or tremor may take the place of athetosis. Spasticity is a result of involvement of the pyramidal tracts, while the involuntary movements indicate that the basal nuclei of the brain are affected.

The cause of congenital cerebral diplegia is a matter of contention. Hemorrhage is the cause usually given; but Collier, in a recent article, has combated this view with great vigor. The very symmetry of the symptoms is not in accord with the irregular way in which hemorrhage usually occurs. It is not possible to imagine a hemorrhagic involvement that would produce the picture of diplegia. The findings in the few cases that have come to necropsy are not those which follow hemorrhage, but consist of an agenesis often with arrest

at a stage of development which is earlier than that at birth. There is no reason to believe that a small meningeal birth hemorrhage would be followed by a general cerebral atrophy. The etiologic factors are therefore unknown; this may be an unsatisfactory conclusion but it is one that applies to many other neurologic conditions such as mental deficiency, spina bifida, muscular atrophy and dystrophy, epilepsy, etc. We need more research in this field of neurology.

THE EFFICACY OF SURGICAL TREATMENT OF SPASTIC PARAPLEGIA. Presented by DR. L. R. ABBOTT (by invitation).

The results obtained at the Shriner's Hospital for Crippled Children and elsewhere were given by the speaker. The procedure most commonly employed by him has consisted of partial peripheral neurectomy of the nerve branches supplying the most spastic muscles, thus effecting a closer approximation to normal muscle balance. Dr. Abbott stressed the importance of postoperative care of these patients, including massage, hydrotherapy, electrical treatment and training. Very little can be accomplished where the cooperation of the patient is not obtainable. As was mentioned in the two preceding papers, the mentality of these children is often much higher than appears at first sight.

SOME PHASES OF INFANTILE SPASTIC PARALYSIS. Presented by DR. T. C. HEMPELMANN.

Only the patient paralyzed from birth or occurring within the first few days of life, are considered in this paper. Since there have been several recent articles (mentioned by Dr. Alford in his paper) which have questioned the etiologic relationship of intracranial hemorrhage and the later development of spastic paralysis, a brief summary was given of the clinical evidence on which pediatricians base their contention that intracranial hemorrhage occurring at or near the time of birth is a frequent cause of this condition. It is a relatively common experience to find babies born that a difficult labor asphyxiated, or cyanotic at birth, drowsy or apathetic, not nursing well, showing disturbances of respiration and often convulsions. A similar picture may be presented some time after birth, as part of the hemorrhagic disease of the new-born infant. There may or may not be a bulging fontanel, but lumbar puncture will usually show a bloody spinal fluid. Should such babies die, necropsy shows an intracranial hemorrhage of variable extent, and therefore when a similar train of clinical symptoms is followed by recovery and the subsequent development of spastic paralysis, it seems natural to assume an identical etiology. The disease often affects all four extremities because following the cerebral trauma an arrested development of the brain, meningoencephalitis, atrophy and sclerosis or other cortical changes result. Usually, however, careful examination will reveal that one side of the body is more affected than the other, and often the intelligence is quite good. The arms may escape the paralysis entirely, but this is rarely, if ever, true of the legs. Often there are periods of fairly good relaxation, but excitement or other emotions cause an exaggeration of the spasticity. Athetosis seems to give a poorer prognosis than simple spasticity.

A less common result of intracranial hemorrhage is marked hypotonia of the muscles, with exaggerated mobility of the joints, delay in walking and talking, and in the later stages, slow, slurring speech and ataxia of the cerebellar type. Such defects are believed to be due to cerebellar injury, possibly associated with lesions of the cerebral hemispheres as well, and offer a much better prognosis as regards the ultimate outcome than the spastic variety of paralysis. Neurectomy and subsequent strengthening and reeducation of muscles, as outlined by Dr. Abbott, have given surprisingly good results even in many patients with the severe spastic condition.

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